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CURRENT CONCEPTIONS ON THE GENESIS OF VESTIBULOVEGETATIVE DISORDERS IN WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 3-10

[Article by B. I. Polyakov, submitted 11 Jan 78]

[English abstract from source]

The up-to-date hypotheses of the genesis of vestibulo-vegetative disorders in weightlessness are taken under critical analysis. Preference is given to the concept which attaches greatest importance to the changes in stereotyped interactions of analyzers responsible for space perception. It is, however, emphasized that neither hypothesis can account for all the phenomena seen in crewmembers in orbital flight. It is, therefore, indicated that mechanisms of vestibulo-vegetative disorders need further study. It is believed that the most promising line of research is to study the role of endogenous factors determining individual variations of motion sickness susceptibility.

[Text] Experience has shown that approximately every third cosmonaut experienced varying degrees of motion sickness during flights, ranging from unpleasant sensations of heaviness in the abdomen to nausea and vomiting. They appeared at different times (from the first minutes to the 7th day) and lasted for different times (from 3 h to several days). In all cases, development of these symptoms was related to abrupt movements of the head, particularly on the first day of the flight.

The pharmacological agents against motion sickness tested under ground-based conditions did not always elicit a preventive and therapeutic response in weightlessness. It was also not always possible to predict endurance of space flight conditions on the basis of the results of preflight vestibulo-metric tests.

All this is indicative of the urgency of the motion sickness problem in space medicine and of a need to continue investigation thereof.

In spite of periodic discussion and some efforts to generalize the accumulated findings, the problem of motion sickness is characterized by a disproportion between the number of facts obtained and theoretical substantiation thereof, the existence of contradictory hypotheses and interpretative systems in

gaining understanding of the nature of this state, and this retards continued development of the problem, making it difficult to resolve the corresponding practical problems.

The research of I. I. Bryanov et al. [1] was among the studies dealing with analysis of the mechanisms of origin of vestibulovegetative disorders in cosmonauts in weightlessness. These authors expound the thesis that impaired hemodynamics, with certain microcirculatory disorders on the tissular and intercellular levels, hypertensive direction of changes, impairment of fluid-electrolyte metabolism with tissular imbalance of potassium and calcium ions created the most beneficial background for development of vestibulovegetative disorders in weightlessness. They believe that, against this background, there can be development of marked reactions, even to threshold and subliminal vestibular stimuli induced by movement of the head and trunk during space flights.

Hence, the authors still believe that vestibular stimulation is the immediate cause of disorders, and they relegate the role of predisposing factor to the hemodynamic changes.

The authors do not refute other conceptions of the genesis of vestibulovegetative disorders in weightlessness, and merely try to enlarge them.

Some examples from clinical practice, the results of special research and reports of cosmonauts served as the basis for the hypothesis of I. I. Bryanov et al. Let us consider the argumentation of these authors, which is based on the following facts.

We know from the literature that there is a link between the state of hemodynamics and state of the vestibular system. We also know of vestibular disturbances in the presence of the hypertensive syndrome and static phenomena, with plethora of cerebral vessels. To this we can add that vestibular nuclei have the most profuse vascularization per cubic millimeter, and they are very sensitive to decreased circulation.

Illusory sensations of upturned body, vertigo and even slight nausea upon moving the head and eyes to extreme positions abruptly have been observed in ground-based studies, on the first few days of clinostatic and anti-orthostatic [head down] hypokinesia. There was intensive manifestation of vestibulovegetative reactions to rather moderate caloric stimulation, which the authors attribute to typical hemodynamic changes indicative of elevation of intracranial pressure and labored venous efflux.

It must be noted, however, that the conditions of afferentation from the otolith system are different in antiorthostatic position than with the head in the usual position, and this factor in itself could change the nature of the reaction referable to the ampullar system.

The periods of maximum severity of vestibulovegetative disorders and symptoms due to redistribution of blood into the upper half of the body (sensation of

blood rushing to the head, heaviness of the head, headache, hyperemia of the sclera, conjunctivitis) coincide. The authors tend to see a link between the two sets of phenomena, and this is quite logical if we consider the above-described clinical and laboratory observations. However, it would be desirable to have additional evidence of the existence of a causative link, rather than only a coincidence in time of appearance of hemodynamic changes and vestibulovegetative disorders during space flights. It can probably be obtained by conducting special investigations, in which redistribution of blood in weightlessness would be excluded or compensated, for example, by means of lower body negative pressure. If the hypothesis of I. I. Bryanov et al. is confirmed, this procedure could also be used as a means of curbing vestibulovegetative disorders in cosmonauts.

It would also be desirable to compare the incidence of vestibular disorders in cosmonauts who did and did not undergo conditioning for antiorthostatic position on the ground.

Finally, it should be noted that the above-mentioned cerebral symptoms are not necessarily associated with vestibulovegetative disorders, as was the case, for example, among the crew of the Salyut-3 station [2].

The American astronaut Sheppard, who suffered from Meniere's disease prior to his flight, did not experience vestibulovegetative disorders in flight after shunting of the endolymphatic sac.

This fact merits attention, although it is not unique. At any rate, the search and trial in weightlessness of agents that regulate intralabyrinthic pressure are considered desirable.

We know of impairment of fluid-electrolyte metabolism in the presence of vestibulopathies and diseases similar to Meniere's disease. Vestibular disturbances were rather marked in cosmonaut Irwin, who presented a potassium ion deficiency during his flight (Apollo 15).

The authors call attention to this fact, although its significance is not quite clear. We are not aware of any convincing data concerning a link between a potassium ion deficiency and degree of predisposition to vestibulovegetative disorders. On the contrary, I. K. Zyuzin [3, 4] has shown that the concentration of potassium ions is not low, rather, it is high in the blood of individuals with a predisposition to motion sickness. Moreover, it must be borne in mind that, in vestibular crises, there is prevalence of vagal symptoms with accumulation in blood of free acetylcholine [5], the effect of which is potentiated by the presence of potassium ions. Consequently, there are no sufficient grounds to assume that, in astronaut Irwin, the shortage of potassium ions was instrumental in onset of vestibulovegetative disorders.

In spite of the debatable nature of some theses, the hypothesis of I. I. Bryanov et al. merits attention and further development. The assumption that hemodynamic changes play the role of a predisposing factor for

development of vestibulovegetative disorders in weightlessness is not unfounded, and it enlarges upon existing conceptions. Moreover, this hypothesis also merits approval because it gives an impetus for broad discussion of such a pressing and vague issue as the pathogenesis of vestibulovegetative disorders in weightlessness, as well as new research, and it ultimately stimulates development of this branch of knowledge.

The views of M. B. Zabutyy [6], based on data in the literature, are in contradiction with the above conceptions. M. B. Zabutyy writes: "... The set of symptoms of motion sickness, which appears in weightlessness, as in other forms of motion sickness, is based on functional disturbances of the vestibular analyzer, namely: 1) attenuation of inhibitory influence of otoliths on the function of receptors of semicircular canals--enhancement of function of the latter; 2) enhancement of function of the vestibular system as a whole under the influence of possible Coriolis accelerations; 3) unusual contradictory information from the right and left labyrinths, which induces in the cerebral cortex and subcortical elements a "collision" [conflict?] between conceptions of spatial body position and corresponding sensory and vegetative reactions, including certain hemodynamic changes; 4) disturbances, which intensify this "collision," referable to interaction between systems of analyzers that implement statokinetic stability, retention of equilibrium and spatial conceptions."

Unfortunately, M. B. Zabutyy does not substantiate his views, although the need for backing them up is obvious. First of all, there must be more definition of the nature of interaction between the otolithic and cupular systems in weightlessness. This is among the least studied questions in physiology of the vestibular analyzer. While the very fact of modulation by the otolithic system of reactions induced by stimulation of the semicircular canals is unquestionable, the specific mechanisms and distinctions of these influences are unclear. Numerous investigations, involving the use of diverse objects and forms of stimulation of the otolith system, under both the combined and successive effect of linear and angular accelerations, revealed that the direction and extent of change in different parameters of the nystagmic reaction depend on the correlation between stimuli in time, as well as orientation of otolithic maculae in relation to the gravitation vector, sign and magnitude of the latter [7-22]. The conclusions of different authors are contradictory.

On the basis of the foregoing, it can be concluded that the conception of constant inhibitory influence of otoliths on the cupular system under ordinary conditions, as well as disinhibition of the latter in weightlessness, is apparently somewhat oversimplified, especially since attenuation of semicircular canal reflexes is observed, rather than disinhibition, in studies involving rotation of subjects in weightlessness [23, 24]. American researchers [25] also confirmed that the sensitivity of the cupular system not only fails to increase, but may even decrease in weightlessness.

It should also be borne in mind that accelerations that are commensurate with those associated with lift-off can induce substantial and rather persistent disturbances (depression) of vestibular reflexes [26, 27] and lower vestibulovegetative stability [28].

Thus, the first of the factors that are, in the opinion of M. B. Zabutyy, the basis of the set of symptoms of motion sickness in space cannot be accepted as conclusively proven.

The second of the listed factors, the possible influence of Coriolis' accelerations, also cannot be accepted since, according to estimates, the magnitude of the above accelerations, which incidentally may only occur periodically, is tens of times lower than the thresholds of sensitivity of the vestibular system [29-33]. At the same time, the thresholds of excitability of the vestibular system either fail to change or increase in weightlessness [25].

The role of contradictory information from the left and right labyrinths in weightlessness is questionable. The very possibility of manifestation of this factor is only theoretical, and it is based on the assumed difference in weight of the otoliths on the right and left sides [34]. However, this should lead to manifestation of very specific tonic labyrinthine reflexes, imbalance of muscle tone on the left and right, impairment of the electrooculogram and other disturbances, which were not actually observed [35].

Unlike the foregoing one, there is no question of the reality of the factor of impaired interaction in weightlessness between analyzer systems involved in statokinetics. There has been repeated indication of the role of this factor [36-38 and others], and at the present time these conceptions are the most acceptable.

The prerequisites for development of these views were supplied by the work of our outstanding physiologists. In particular, I. P. Pavlov and his disciples, who studied the synthetic conditioned reflexes and phenomena of the dynamic stereotype, demonstrated that the synthetic complex nature of stimuli, their spatial and time-related stereotypic nature, is the most typical of environmental conditions. Any exogenous stimulus always reaches a "solid" that has been prepared by the entire aggregate of prior stimuli [39]. The responses of the organism are, therefore, the result of integration of signals from different stimuli or components thereof.

L. A. Orrell [40] called such phenomena "interaction of afferent systems," and he believed that the principle of analyzer interaction is the dominant one in the function of the central nervous system (CNS), which was confirmed by subsequent investigations [41-49, 51].

In the light of the foregoing, the function of the vestibular analyzer cannot be considered separately, apart from its correlation with other, functionally related analyzer systems (visual, proprioceptive, etc.). Under ordinary conditions, these analyzer systems are functionally coordinated, providing

the CNS with mutually supplementing and correlating signals about the position of the body in space, as validly indicated by G. L. Komendantov [50]. Disruption of the customary information stereotype could induce unusual neuroreflex reactions.

The results of the research of M. D. Yemel'yanov and A. G. Kuznetsov [51] served as one of the first practical confirmations of this thesis; they demonstrated that the thresholds of some vestibulovegetative reflexes can be lowered under the influence of stimulation of other afferent systems (visual or proprioceptive). For this reason, the principle of interaction of analyzer systems was applied to interpret the genesis of motion sickness.

Somewhat later, Lansberg [52], who analyzed the data of different authors, arrived at the conclusion that an "intralabyrinthine conflict," induced by different impulsation from the otoliths and semicircular canals, is the cause of motion sickness. Such a situation occurs, for example, when the head is tilted forward and backward after rotation. In such cases, the usual (unchanging) impulsation from the otoliths is combined with impulsation from the semicircular canals, which is altered by prior rotation. There is impairment of the usual stereotype of stimuli from different parts of the vestibular system.

The structure of the stimulus that occurs with concurrent rotation in two planes, for example head tilting during rotation in a chair (expert vestibulometric test), is another example of canal-otolith conflict. When the head moves, the otoliths send signals about the tilting along one axis, whereas the semicircular canals send signals at this time about angular acceleration along an axis that is approximately perpendicular to the first one. Under natural conditions, this type of sensory information is impossible, since otherwise movement of both halves of the skull should be in different directions [37].

There are other forms of sensory conflict, other than that between the canals and otoliths, that could lead to motion sickness [37].

The visual-proprioceptive and canal-otolithic systems deliver to the CNS contradictor or uncorrelated information simultaneously. There has been repeated demonstration of the pathogenicity of such a situation [38, 53, 54 and others].

The visual system sends signals to the CNS that are not accompanied by the corresponding information from the proprioceptive and vestibular systems.

Vestibular and proprioceptive information is not accompanied by the corresponding information from vision. Such a situation is formed in the closed cabin of an aircraft or ship. In such a case, the inertional receptors send signals about movements of an object, while the eyes supply information to the effect that there is no movement in relation to the ambient situation. Occasionally, even experienced pilots who have learned to integrate visual and inertional signals that are inherent in flight

suffer from motion sickness when they are passengers (deprived of the customary visual reference points).

Thus, the essence of the sensory conflicts lies in the fact that information from the vestibular system and other functionally related sensory systems is in contradiction with the integral sensory image (nerve model) of the complex stimulus inherent in body movement in space, which was formed on the basis of prior experience.

An analogous phenomenon could occur in weightlessness. When there are head movements under space flight conditions, the semicircular canals are stimulated just as they are on earth, while the otolithic receptors are stimulated in an unusual way, since the pulses of linear accelerations are not associated with the customary gravitational vector, which is lacking in weightlessness. There is similar lack of coordination of signals in the visual-proprioceptive system. The new integral sensory image than then appears is in contradiction with the one formed under ground-based conditions.

In the opinion of L. A. Kitayev-Smyk [55], the neuropsychological system of probabilistic forecasting is involved in forming man's reaction to weightlessness [56, 57]. The new integral sensory image of space emits signals about an improbable (unpredictable) situation from the standpoint of individual experience, in response to which the body does not yet have formed behavior programs that are stored in memory. Under such conditions, some individuals may develop various nonspecific forms of defense reactions, including motion sickness.

We also know of an original hypothesis of weightlessness as a distinctive "minus stimulus" of the otolithic system [58]. It is based on the results of studying the distinctions of nystagmus in weightlessness and increased weight. It was found that in weightlessness there is a decrease in post-rotational nystagmus, but under the influence of accelerations (in a centrifuge) there is an increase in intensity of caloric nystagmus.

On the basis of conceptions of the inhibitory effect of otoliths on function of the cupular motion, the author concludes: "... Weightlessness does not lead to functional exclusion of the otolithic system or physiological de-labyrinthization thereof; rather, it is a unique minus stimulus that causes specific vestibular reactions."

In interpreting the results of these studies, in addition to the above-noted differences in types of interaction between the otolithic and cupular systems, it could be assumed that intensification of caloric nystagmus with increased gravity is related to intensification of convection flow in the endolymph, which is the basis of caloric stimulation of the labyrinth.

To sum up the foregoing, we can state the following:

1. The problem of human "stress" is still one of the most pressing problems of space medicine.

2. The symptoms of motion sickness in weightlessness are related to stimulation of the vestibular system with natural head movements; predisposing factors, such as hemodynamic changes, play some role.

3. There are several hypotheses concerning the pathogenesis of vestibulo-vegetative disorders in weightlessness. The most substantiated one is the conception of the role of disturbances in the customary stereotype for ground-based conditions referable to interaction of analyzer systems that implement spatial perception (sensory conflict).

The hemodynamic change that is typical in weightlessness may be another pathogenetic factor. However, the significance of this factor, as compared to sensory conflict, is not quite clear and should be the subject of future investigations.

4. None of the existing hypotheses can explain the entire aggregate of observed phenomena.

It is desirable to consider this matter from the positions of theory of functional systems [59]. This is hampered by the lack of formed conceptions about the activity of a statokinetic functional system (principles of integration of signals in the course of afferent synthesis, decision making, the other mechanisms of systemic organization).

5. Heretofore, researchers have concentrated mainly on the conditions under which the vestibular analyzer functions in weightlessness as an unusual habitat, and on other exogenous factors. Yet the question of why, in spite of dissimilar environmental conditions, vestibulovegetative disorders do not occur in all cosmonauts, but only in some of them, remains open. This question is not quite clear either for living conditions on the ground, and this is indicative of a need to investigate the role of endogenous factors, i.e., the clinicophysiological distinctions of the integral organism that predetermine resistance or, on the contrary, susceptibility of man to motion sickness.

Whatever the views of researchers concerning the mechanism of vestibulo-vegetative disorders in weightlessness, the problem of causes of individual differences must be solved.

Concurrently with continued investigation of the mechanisms of the statokinetic system, distinctions of its function in weightlessness, as well as the role of the hemodynamic factor, it is imperative to refine methods of occupational screening and to use test factors that are more similar to real stimuli present in flight. There is still an urgent need to find effective agents for the prevention and treatment of motion sickness. Investigation of the causes of individual differences in degree of predisposition to motion sickness in different people is the most promising direction of research which, in our opinion, is of key importance to the solution of the problem as a whole.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 612.46-06:[612.273.2+612.766

EFFECT OF HYPOXIA ON FLUID-ELECTROLYTE METABOLISM AND RENAL FUNCTION IN MAN AS RELATED TO DIFFERENT DEGREES OF MOTOR ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 10-14

[Article by A. I. Grigor'yev, V. I. Korol'kov, G. I. Kozyrevskaya and M. A. Dotsenko, submitted 14 Mar 77]

[English abstract from source]

It was demonstrated that a prolonged (24 days) bed rest at altitudes of 2200 m and 3000 m as well as at sea level was accompanied by an increased renal excretion of fluids and osmotically active substances, including electrolytes. Exercises done during bed rest induced a similar increase of the renal excretion of sodium and potassium. However, as bed rest continued the differences between the groups of test subjects disappeared. The levels of oxygen and glucose used in the study proved insufficient to prevent changes in the fluid-electrolyte metabolism occurring during bed rest.

[Text] In the case of prolonged bed rest, there is increased excretion of fluid and electrolytes by the kidneys, as is the case during a space flight, and this leads to development of negative balance thereof. This could be the cause of numerous functional disorders. In the opinion of some researchers [1, 2], the use of various gas atmospheres (including a hypoxic one), which increase the body's resistance to some extreme factors and prevent a number of adverse changes in fluid and electrolyte metabolism, is of interest in this respect.

Our objective here was to test the effect of a prolonged stay at high altitude on man's fluid-electrolyte metabolism and renal function during bed rest with different amounts of exercise.

Methods

We selected 12 essentially healthy men ranging in age from 18 to 25 years to participate in this study; they were conditioned and resistant to hypoxia to about the same degree.

After two background examinations at the therapeutic clinic of Frunze Medical Institute, all of the subjects were transported to the mountains at an altitude of 2200 m, then in horizontal position to an altitude of 3200 m. They spent 12 days at each altitude, and overall duration of bed rest in the mountains constituted 24 days.

During the stay in the mountains, the subjects were separated into two equal groups, according to degree of motor activity: the first group consisted of subjects on strict bed rest (clinostatic hypokinesia) and the second, subjects submitted to measured exercise against the background of bed rest. For partial compensation of motor inactivity, the second group of subjects performed exercises in two cycles, lasting a total of 40 min, with total energy expenditure of about 300 kcal/day, while remaining in horizontal position [3].

The subjects spent 10 days at a hospital (in Frunze) after the bed rest, with unrestricted motor activity (recovery period--RP). At all stages of the study, the subjects were on a standard diet consisting of natural foodstuffs with a caloric value of about 3000 kcal/day.

In order to assess fluid-electrolyte metabolism and renal function, we weighed the subjects, assayed sodium and potassium concentration in blood serum and urine by the method of flame photometry, osmotic concentration using a semiconductor thermistor, creatinine content according to Bonsnes-Toski, hematocrit, circulating plasma volume using Evans' blue (T-1824), and renal plasma flow with 70% diiodone [cardiotrast] by the method of Smith-Ratner. We kept a record of daily fluid input and output. In addition, we calculated circulating blood volume and erythrocyte mass, rate of glomerular filtration according to endogenous creatinine clearance, renal blood flow and resistance to blood flow in the kidneys.

A 4-h water load test (20 ml/kg body weight) using the conventional method was performed in order to assess osmoregulatory function of the kidneys. Determination was made of osmotic index, osmotic clearance, clearance of osmotically free fluid and rate of excretion of osmotically active substances at the height of fluid diuresis, as well as with spontaneous diuresis [4, 5].

Results and Discussion

In the background studies, the parameters of fluid-electrolyte metabolism and renal function were consistent with the levels inherent in a healthy man under analogous climate conditions.

During the stay in the mountains, both groups of subjects lost weight to a mean of somewhat more than 2 kg by the end of the experimental period. A change in fluid balance during bed rest could be one of the possible causes of this phenomenon [6]. Apparently, hypohydration of the body could be considered the chief cause of weight loss, in view of the fact that the weight of the subjects virtually returned to base levels by the

3d day of the RP. The data pertaining to daily fluid intake and output could serve to confirm this assumption. During the stay in the mountains, both groups of subjects presented virtually the same decrease in fluid intake ($P=0.05-0.01$). In spite of this, there was a mean 250 ml ($P<0.05$) increase in diuresis during the period of bed rest in the first group of subjects, and virtually no difference from the base level in the second group.

Of course, the changes in absolute fluid input and output in the course of the study caused changes in renal loss of fluid (ratio of diuresis to fluid intake) [7]. Thus, while the magnitude of this parameter did not exceed levels that are usual for these climatic conditions (51-63% of total 24-h fluid intake) in the background tests, during the period of the study it increased to a mean of 74-82% in both groups of subjects (Figure 1a). At an altitude of 2200 m, renal fluid loss was greater in the first group of subjects ($P<0.05$), while no differences between indices of both groups were demonstrable at an altitude of 3200 m.

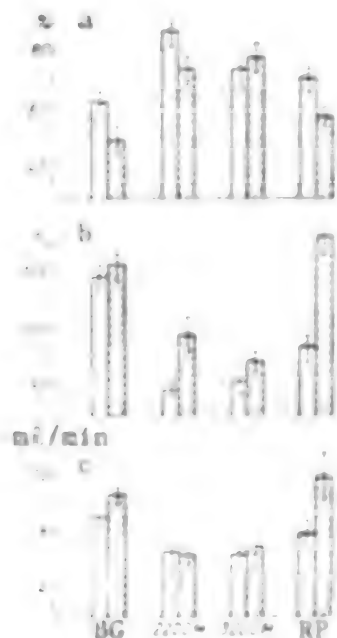


Figure 1.

Ratio of diuresis to total fluid intake (a), fluid output after water load (b) and excretion of osmotically free fluid during maximum diuresis (c) in the two groups of subjects at different stages of the study. Here and in Figures 2 and 3: white columns, 1st group; striped columns, 2d group; BG, background; RP, recovery period.

Along with increased diuresis during bed rest, both groups of subjects presented an increased rate of electrolyte excretion by the kidneys. The increase in renal excretion of sodium was substantial, both at 2200 m ($P<0.01$) and 3200 m ($P<0.05-0.01$). Natriuresis was more marked in the first group (Figure 2a). At the end of the study period, at an altitude of 3200 m, we observed relative sodium retention, particularly in the 2d group of subjects, but excretion remained high in comparison to the base levels ($P<0.05$). In view of the fact that there was virtually no change in filtration charge of sodium during the study in both groups of subjects, the increase in excretion thereof was the result of decreased reabsorption of this ion in the renal tubules. As a result, we demonstrated an increase in fraction of excreted sodium from a mean of 0.68 ± 0.02 to 1.02 ± 0.09 and from 0.58 ± 0.03 to 1.03 ± 0.08 ($P<0.01-0.001$) in the 1st and 2d groups, respectively.

During bed rest, there was also an increase in excretion of potassium (Figure 2b). However, these changes reached statistical reliability only during the second half of the study in the 1st group of subjects.

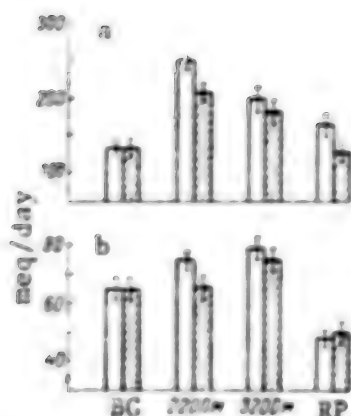


Figure 2.

Renal excretion of sodium (a) and potassium (b) in both groups of subjects at different stages of the study (M±m)

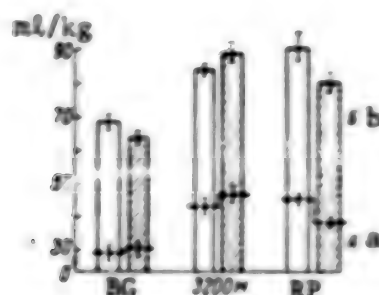


Figure 3.

Change in volume of circulating blood (a, below line) and volume of erythrocyte mass (b, above the line) in both groups of subjects at different stages of the study (M±m)

($P < 0.05$), and this is apparently related to decrease in muscle weight during prolonged hypokinesia. Analogous changes in potassium excretion were observed during bed rest in the lowlands [6].

The above changes in osmoregulatory and ionoregulatory function of the kidneys could be related to the distinctions of renal hemodynamics or state of neurohumoral systems that maintain fluid-electrolyte homeostasis of the body's endogenous environment. Since no substantial changes were demonstrated in rate of glomerular filtration or renal blood flow throughout the period of the study, with the exception of faster glomerular blood flow on the 1st day of bed rest ($P < 0.05$), the increased excretion of fluid and electrolytes was attributable to a change in transport thereof in the tubules.

Under these conditions, decreased activity of the renin-angiotensin-aldosterone system, which was repeatedly observed with man in a horizontal position [1, 9] and under hypoxic conditions [10-12], could be the most probable cause of decreased reabsorption of fluid and sodium. Since changes in intravascular volume and electrolyte composition of blood could be the chief factors affecting the decrease in secretion of renin and aldosterone during bed rest and stays at high altitudes, special attention was devoted to these problems.

We observed a significant ($P < 0.01$) increase in circulating blood volume (Figure 3a) in both groups of subjects during the stay in the mountains. This was not associated with significant change in plasma volume, and the observed hypervolemia was attributable mainly to an increase ($P < 0.001$) in erythrocyte mass (see Figure 3a). In addition, there was an increase in sodium concentration in blood plasma ($P < 0.05$) during the period of the

investigation. The increase in circulating blood volume and concentration of sodium in plasma could be the cause of decreased renin and aldosterone production [11, 12] and, consequently, increased renal excretion of sodium and fluid.

We conducted a functional test with a water load for the purpose of more comprehensive examination of the functional state of the kidneys; it revealed a decrease ($P < 0.05-0.01$) in fluid output (Figure 1b) in all subjects at both altitudes. At 2200 m, the 1st group of subjects presented a greater decrease in fluid excretion after the water load than the 2d group ($P = 0.05$). This was apparently due to more marked hypohydration of individuals who maintained strict bed rest. At 3200 m, no differences were demonstrated between the groups with regard to the water load test.

Along with a decrease in renal capacity to rapidly excrete fluid after the water test in both groups of subjects, there was a decrease ($P < 0.05$) in maximum diuresis and excretion of osmotically free fluid (Figure 1c) during the study period, which was most likely indicative of incomplete depression of antidiuretic hormone secretion after the water load. At the peak of fluid diuresis, we observed an increase ($P < 0.01$) in osmolarity of urine and, consequently, in value of the osmotic index ($P < 0.01$). Evidently, these changes in osmoregulatory function of the kidneys could be the result of relatively high secretion of antidiuretic hormone during bed rest, at the stage prior to the test, due to the above-mentioned increase in osmotic concentration of plasma and increase in sodium content thereof. At the same time, prolonged exposure to hypoxia in the case of ordinary motor activity does not activate the antidiuretic system and could even reduce antidiuretic hormone production [13].

Thus, our investigations established that 24-day bed rest at a high altitude, like hypokinesia at the usual barometric pressure, induced an increase in renal excretion of fluid, osmotically active substances, sodium and potassium in essentially healthy people. Hypohydration of the organism (about 3-4% of body weight) was the result of increased excretion of fluid. However, while dehydration was associated with a decrease in circulating blood volume under lowland conditions, in the presence of hypoxia we observed an increase in blood volume due to increase in erythrocyte mass. The set of exercises performed at high altitudes during bed rest resulted in less marked increase in excretion of fluid and electrolytes only at an altitude of 2200 m. With a longer stay in the mountains, no differences in osmoregulatory and ionoregulatory renal function were noted between the two groups.

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POSSIBILITY OF USING BONE CONDUCTION IN AVIATION RADIO COMMUNICATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 14-19

[Article by E. V. Lapayev, V. S. Kuznetsov, G. I. Tarasenko and M. I. Katalov, submitted 26 Oct 77]

[English abstract from source]

A combined use of adapted antinose devices and a bone transducer makes it possible to provide a better quality of speech perception under noise conditions. The frequency characteristics of the bone transducer depend on its location and configuration.

[Text] Many works by Soviet and foreign authors deal with demonstration of the mechanisms of bone conduction [1-9]. However, the dissemination of verbal sounds emitted by man over the cranial bones has not been sufficiently investigated.

Our studies of bone conduction provided for enhancement of the quality of speech perception and reproduction over communication channels equipped with noise-suppressing devices.

According to the data of Martin [10], Goodhill et al. [11], placement of bone telephones in the region of the forehead is the most convenient and promising. These points were chosen for the purpose of delivering the verbal signal to the organ of hearing. The experience of clinical examination of patients and use of hearing aids revealed that the region around the ear (mastoid, conchal tragus) is the most convenient for placement of electroacoustical transducers [transformers]. In our work, we studied the nature of generation of a verbal signal by the articular system, extending through the cranial bones (microphone channel) and distinctions of auditory perception of a verbal signal through bone (telephone channel).

Methods

We selected eight regions on the surface of the head for our studies: the cheek, upper lip, forehead, occiput, chin, mastoid, conchal tragus and parietal region, where a standard bone "sensor" as used in hearing aids and audiometers was placed.

The syllabic articulation tables (GOST 16600-73) read by experienced speakers in a quiet environment and with noise of 120 dB were recorded synchronously by means of the condenser microphone and bone "sensor" on two identical tape recorder tracks [channels]. The obtained verbal material was analyzed by a trained articulation team in order to determine the clarity of syllables obtained with the use of the selected regions for the location of the bone "sensor."

The spectra of speech were examined to assess distortions appearing along the osseous route of reproduction of the verbal signals, as compared to the usual air route.

Since there are great difficulties involved in obtaining a precise record of the distinctions of frequency characteristics of osseous "sensors" [or pickups] loaded for external impedance, we used the method of comparison of spectra of speech oscillations from the bone "sensor" and air microphone to determine the spectral features of speech. For this purpose, we recorded the standard phrase, "one... two... three...", on both channels of the tape recorder, as pronounced by the speaker before and after reading the syllable tables. We then made a frequency analysis of the standard phrase on a spectrometer in one-third octave bands. The frequency spectra of the test [standard] phrase from the bone "sensor" at each tested point were scaled to the spectrum obtained from the microphone by calculating the difference between intensity of the verbal signal through bone and air in identical one-third octave filters.

The same device was used to assess the transmission-frequency characteristics of bone conduction of a verbal signal from the region of the forehead. In this case, the bone "sensor" was replaced by an accelerometer which had uniform frequency characteristics from 5 to 20,000 Hz. Phonemes (a, o, u, y, i) were used as signals, as uttered by the speaker and recorded on tape. This was followed by harmonic spectral analysis of the verbal phonemes. The transmission-frequency characteristics of bone conduction were defined as the difference between signal levels at a given frequency in the channel of the accelerometer and microphone.

In order to explore the possibility of using bone conduction for perception of speech, the bone "sensor" operating in the telephone mode was fixed on the tested places of the human head, and standard syllable tables were transmitted from the tape recorder, through an amplifier. The effectiveness of perception of verbal material was determined by the quality of intelligibility.

With the use of noise, the bone "sensors" were protected by various noise-proof devices (plugs, helmet, noise-proof mask), which enabled us to assess the prospects of practical use of a bone "sensor" in modern communication systems. It was of special interest to investigate the effect of occlusion, which occurs when the external auditory meatus is blocked by ear plugs, as a means of improving auditory perception.

Results and Discussion

The Table summarizes the results of articulation readings obtained with the use of a bone "sensor" in the microphone mode. The data listed in this table indicate that the intelligibility of syllables in the verbal signal recorded with the bone "sensor" is in the range of 58 to 73%, depending on where it is placed. These grades of intelligibility are 11-26% lower than those obtained for the same tables recorded on the second channel of the tape recorder through air microphones. The difference is somewhat smaller in the case of intelligibility of words, obtained by estimation, due to the extra information contained in words.

Intelligibility of speech as related to the place where the signal is picked up by a contact "sensor" and type of microphone

Type of microphone, air and bone conduction	Point at which sig- nal is picked up by "sensor"	Intelligibility of verbal signal, %			
		syllables		words	
		quiet	noise, 120 dB	quiet	noise, 120 dB
Condenser microphone	—	84	—	99	—
DEMSH-14	—	82	34	99	84
LA-5 laryngophone	Larynx	80	30	99	80
Bone sensor	Occiput	66	39*	95	86*
" "	Conchal				
" "	Tragus	58	41*	95	87*
" "	Chin	73	37*	95	85*
" "	Forehead	62	44*	95	89*
" "	Mastoid	66	31*	95	83*
" "	Parietal region	63	31*	95	83*

*Noise-proof device was used to protect the bone "sensor."

In a quiet environment, placement of the bone "sensor" on all of the test points provided for a high grade of communication quality, though somewhat poorer than with air microphones.

There was drastic decrease in intelligibility of speech in the presence of exogenous noise of 120 dB. However, relatively simple protection of the "sensors" from noise by means of existing noise-proof devices and those being developed made it possible to pinpoint the promising places for placing a bone microphone on the human head. In this series of studies, the bone "sensor" was protected by means of a noise-proof mask (on the chin), hard noise-proof helmet (protecting the forehead, occiput and sinciput) and additionally by plugs installed in the helmet (to protect the tragus and mastoid). The obtained results were compared to the intelligibility of verbal material obtained when recording the syllable tables using a DEMSH-1A microphone and LA-5 laryngophone. According to the data

in the Table, when the electroacoustic bone transducer is protected with noise-proof devices, the syllabic intelligibility is 5-15% higher from the regions of the forehead, occiput and conchal tragus than through the DEMSh-1A and LA-5. Studies in this series do not alter existing conceptions [12, 13] that bone microphones have poorer resistance to noise than air microphones, but they show the directions that permit more effective use of bone conduction for practical purposes, by means of an optimum combination of noise-proof devices and bone "sensor."

The Figure illustrates the results of analysis of distortions of the verbal signal of the standard phrase in the frequency range of 160 Hz to 5 kHz, scaled to the spectrum of speech recorded through the microphone channel.

The maximum and minimum differences in air-bone speech transmission, obtained from the results of analysis in each one-third octave filter are shown by the top and bottom boundaries of each graph, which characterizes, to some extent, the error factor of the method. The striped area is the deviation of spectra of the bone "sensor" from the spectrum of the microphone channel. Positive figures indicate that higher levels are picked up from the bone channel in a given one-third octave band than from a microphone.

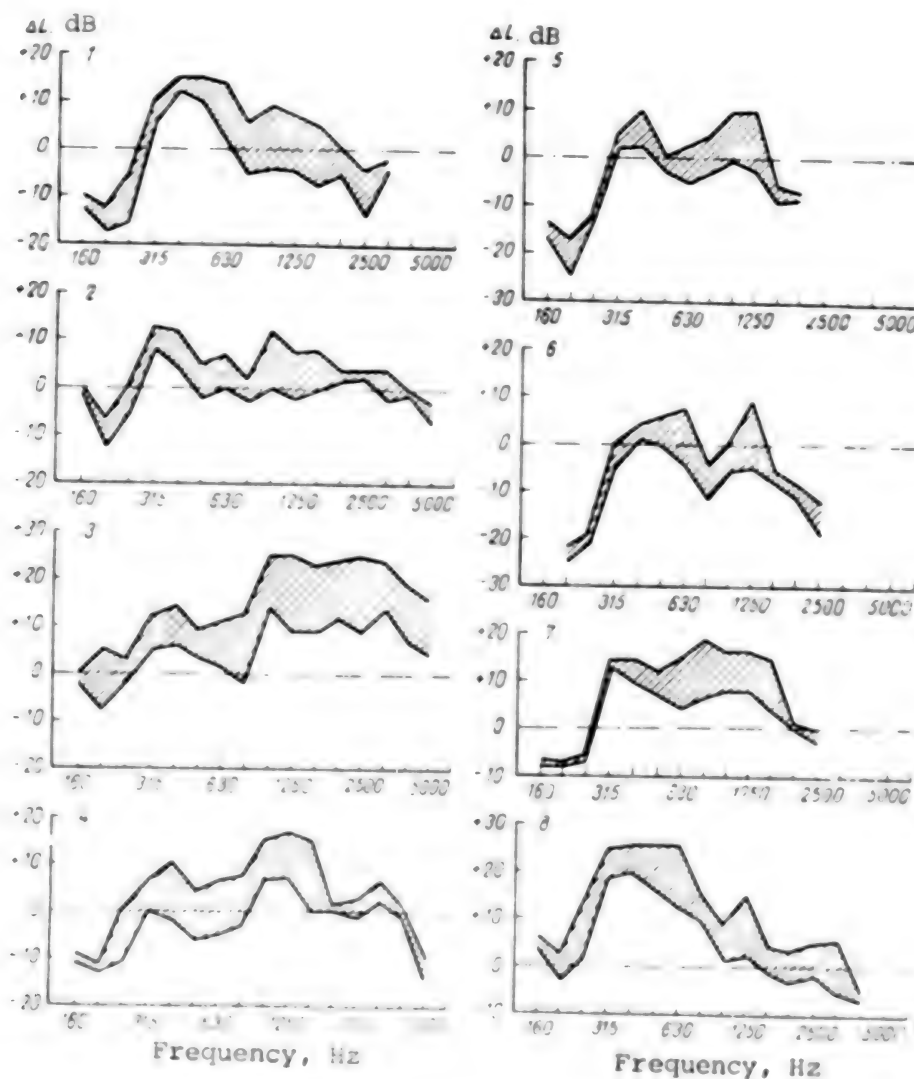
The spectrum of a standard phrase (determined in most cases by the vowel "a") obtained with the bone "sensor" placed on different parts of the head is characterized by certain frequency deviations from the spectrum of speech via the air route of sound conduction. At several points, we observe elevation of components in the region of low frequencies (points 1 and 8, forehead and sinciput); at other points this applied to high frequencies (points 3 and 4, upper lip and cheek) and at others yet the spectrum was close to normal (point 2, chin). The degree of high-frequency transmission is correlated the most with intelligibility.

Analysis of the spectral composition from the bone "sensor" reflects only some of the distinctions of Russian speech. Apparently, other vowels of the Russian language would have a different degree of distortion. Measurement of transmission-frequency characteristics of vowel phoneme sounds and their harmonics was made at fundamental tone frequencies of 101 and 167 Hz. As shown by the measurements, the transmission-frequency characteristics are uneven, with level changes of 30 dB, for all sounds in the above frequency range.

The shape of the curves of transmission-frequency characteristics is specific for each tested sound, and within the range of reading error it is unrelated to the frequency of the fundamental tone, as indicated by the results of measurements taken at different fundamental tone frequencies of the sounds studied.

The causes of variations in transmission characteristics are probably referable to the difference in route traveled by the sounds from the sites of production thereof to the pick-up points, the nature of damping [attenuation]

and resonance phenomena. The data pertaining to transmission-frequency characteristics of bone conduction with the sensor located at any given point should serve as the basis for selection of optimum frequency components of electroacoustical systems used in communications and rehabilitation of hearing.



Spectral characteristics of verbal signal recorded with bone "sensor" from different parts of the head

- | | | |
|--------------------|-------------------|--------------------|
| 1) forehead region | 4) cheek | 7) occiput |
| 2) chin | 5) conchal tragus | 8) parietal region |
| 3) upper lip | 6) mastoid | |

There are considerably more works dealing with bone conduction with the use of a bone "sensor" in the telephone mode [14-17]. In our studies, we confirmed that optimum intelligibility of perceived speech is observed when the "sensor" is fixed on the mastoid, conchal tragus and forehead. Protection of the "sensor" from noise by means of plugs increases intelligibility of syllables by up to 15%. An even better effect is obtained if the auditory meatus is protected with ear plugs. In this case, there is attenuation of noise to which the ear is exposed via air, on the one hand, and increase in concentration of sonic energy in the region of the middle ear as a result of the occlusion effect, on the other, which leads to amplification of the perceived signal. For the forehead, mastoid and tragus, the gain in intelligibility due to occlusion constitutes up to 20% (in the presence of noise). When the bone "sensor" is in the region of the occiput use of ear plugs does not improve intelligibility. Evidently, this is attributable to the anatomical and morphological distinctions of the occipital region, where there is essentially prevalence of compression vibrations of tissues, there being less significance of inertional mechanisms of bone conduction, to which the occlusion effect is related.

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[656.7+629.78]:658.311.44

SPEECH ILLUSIONS AND SIGNIFICANCE THEREOF TO AEROSPACE PRACTICE

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1979 pp 19-21

[Article by I. Shul'ts and M. Moravek,* submitted 2 Nov 77]

[English abstract from source]

The pattern of erroneous perception of intelligible and incoherent words accompanied by loud noise has been investigated. It has been found that proper interpretation of incoherent words depends at large on their rhythmic, or syllabic structure. As a rule, the words are reconstructed in the back to forward direction. One- and two-syllable words with pre-dominant median and low frequencies are those which are most frequently subjected to speech illusions.

[Text] In aviation and cosmonautics, not only the effectiveness of fulfilling the flight program but, to a significant extent, safety of a mission depend on providing reliable communication. It is also known that radio communication between ground-based operators and crew members always takes place against the background of a relatively high level of different types of noise interference. Several flight incidents have been described in the literature, which were related to faulty reception or misunderstanding of a communication [1-3].

We submit here the results of studies pursued to explain the causes of erroneous interpretation of both meaningless and meaningful words. In our opinion, erroneous interpretation of a communication is more important to the safety of a mission than missing it entirely. When a pilot does not respond to inquiries of a ground-based operator, the aviation radio communication system provides for repetition of the message. This opportunity does not exist in the case messages are misunderstood.

Methods

We conducted two series of studies.

In the first series, a tape recording was used to present a series of 20 meaningless words to 56 healthy subjects, the average age of whom was

*CSSR.

32.4 years. Different phonemes were not repeated in the words. When choosing them we adhered to the principle of frequency representation of phonemes and combinations thereof in Czech. The signal to noise ratio during reproduction of the words constituted +10 dB. In all, we presented 1120 spurious words.

In the second series, we tested 80 pilots by the method of aviation speech audiometry. The tape that the pilots listened to was obtained in the following manner: a standard tape recording used in clinical practice was transmitted over a system of three interconnected ground-based radio stations to an aircraft, where it was rerecorded. Thus, we obtained eight variants of a set of words unevenly obscured to different extents by noise. The difference between the verbal signal and noise constituted +3.7 dB, the range being 0-20 dB. The pilots listened to this distorted tape of 100 words through a headset in a quiet chamber at an amplification of +30 dB above the absolute threshold of hearing. In all, 8000 words were presented.

In the tests, we were concerned only with the subjects' wrong answers

Results and Discussion

In the first series of tests, we presented a total of 1120 "words" consisting of 6720 phonemes. Distortions at the lowest level of decoding of the verbal stimulus were noted in 962 cases (14.2%). The different phonemes varied with respect to possibility of "substitution." The vowel sound "a" was found to be the most discernible, and it was properly identified in 99% of the cases. The "substitution" dynamics are interesting. Thus, the phoneme "a" was perceived in rare cases as "e," the phoneme "e" as "o" and "o" as "a." The phoneme "b" was perceived as "p," "p" as "k," "k" as "p," etc.

If an entire word is taken as the main unit, 522 words (46.6%) were perceived with distortion. Some meaning was attributed to almost half of them (222), although the stimulus was meaningless. The syllabic structure of the words was always correctly retained in illusional perception thereof. If only part of a word was correctly perceived, reconstruction of the word was more often determined by the end of the word, although intelligibility of the end of the presented words was greater than of their beginning.

Analysis of the results of the second series of studies revealed that one- and two-syllable words are distorted more often, and three-syllable ones less often. With regard to the height of the formants, most mistakes are noted for "low" words, followed by "average" and least of all in "high" words. With concurrent consideration of syllabic structure and position of the verbal stimulus on the frequency band, we find that the mistake is most often related to perception of two-syllable "medium," one-syllable "medium" and one-syllable "low" words (to 15%). Three-syllable words with prevalence of high formant frequencies are the least susceptible to distortions.

The relative stability of rhythmic structure of words was equally manifested in the first and second series of tests. It consisted of a great similarity of the "syllabic nature" of the verbal stimulus and response. Two-syllable words were the most stable. In our opinion, the tendency to give preference to two-syllable answers, rather than one- and three-syllable ones, reflects the statistical patterns inherent in the Czech language. As in the studies with meaningless words, in perceiving meaningful words the pilots most often correctly picked up the end of the verbal stimulus, as compared to the beginning. Reconstruction of a word in the case of erroneous perception most often occurred starting at the end of the word (54.5%), rather than the beginning (41.1%). In 4.1%, we were unable to determine the source of the verbal illusion; often it was a case of free associations, without any relation whatsoever to the rhythmic or phonetic form of the stimulus.

Unlike the first series, in the second one we were unable to demonstrate a rule for substitution of some phonemes by others in meaningful material. In this respect, our findings differ from those of authors who were concerned with a similar problem in the past [4].

Reconstruction of an indistinctly perceived verbal signal is a complex process [5, 6]. The missing part of the verbal signal, obscured by noise, is filled in on the basis of infraverbal, verbal patterns and on the semantic level, supravocal psychological and linguistic patterns also. It appears that the higher the structural level of the perceived information, the greater the possibility of noise of a biological nature (emotions, fatigue, etc.) and situational context affecting the accuracy of its interpretation. The lower the structural level of the perceived information, the more importance is acquired by rhythmic, phonetic and phonological properties of the verbal stimulus.

Perception of a complex verbal signal is based on successive evaluation of the main units on the lower level of the structure of the message. The syllable is the lowest perceived unit of speech [6]. Setting aside the role of this unit in decoding a verbal signal on the phonetic level, the property of "syllabicity" becomes particularly significant: the rhythmic pattern of verbal structure. According to works dealing with the study of speech perception in the presence of noise, this characteristic is relatively very stable [7].

The tendency to interpret indistinctly perceived words on the basis of their ending could be attributed, at least in part, to the fact that in a situation of informational uncertainty the listener makes a decision about the semantics of the message only after he has picked up the widest possible assortment of informational characteristics (rhythmic, intonational, phonetic, etc.) about the acoustic signal. There is an important conclusion to be derived from these findings for aviation and space radio communication practice. When training operator-speakers for air and space traffic, one must stress the need for proper enunciation of expressly the endings of all words. It is a known fact from experience that many flight controllers and even pilots "swallow" the last syllables.

The overall intelligibility of radio conversations can be substantially improved by selecting a suitable length and frequency composition of words in the aerospace vocabulary. Nevertheless, the above method does not provide in all cases for effective stability of verbal signals with regard to diverse distortions.

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AGE-RELATED DISTINCTIONS OF CHANGES IN PSYCHOPHYSIOLOGICAL FUNCTIONS OF PILOTS IN THE CIVIL AVIATION UNDER THE INFLUENCE OF VIBRATION AND NOISE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 21-24

[Article by Yu. N. Kamenskiy and Ye. A. Sokolova, submitted 20 Dec 76]

[English abstract from source]

The effect of vibration and noise of helicopters on the psychophysiological functions of their crewmembers was studied in relation to their age. The changes were mostly pronounced in pilots younger than 20-25 and older than 45 years. The peculiar changes in the psychophysiological functions can be associated with the age-related features of adaptation to vibration and noise effects and with the different level of professional training.

[Text] The work of helicopter crews presents several distinctions due to the effects of specific flight factors and difficulty of piloting helicopters. Under such conditions, the safety of a flight depends on the pilot's professional skills, his health status, which is largely determined by his age [5] and extent of effects of specific flight factors (noise, vibration). At the same time, there has not been sufficient investigation of the age-related aspect of the influence of vibration and noise on piloting.

Methods

Studies were conducted with civil aviation pilots in the spring and summer, under good weather conditions and microclimate in helicopter cockpits. The pilots of different types of helicopters were divided into six age groups: 20-25 years, 26-30, 31-35, 36-40, 41-45, 46 and older (see Table).

Yak-40 aircraft pilots served as a control group. The working conditions, work and rest schedules were essentially the same for both groups of pilots. Substantial differences were referable only to noise and vibration levels. Thus, according to the data of V. Ye. Kvitka [1], in the crew's quarters of the Yak-40 aircraft, the levels of these factors were below the maximum permissible norms recommended by the International Standard ISO PMS-2631. Conversely, according to the data of I. Ya. Borshchevskiy et al.

[2, 3], as well as N. N. Gurovskiy [4], the vibration in helicopter cockpits exceeded this standard and sanitary norm No 1102-73.

Quantitative distribution of pilots studied in age groups

Age, years	Number of subjects	
	helicopt. pilots	Yak-40 pilots
20-25	25	15
26-30	27	71
31-35	41	50
36-40	21	33
41-45	12	21
46 & older	14	13
Totals . . .	140	203

The pilots were examined in the morning, 30-60 min before flights and in the evening, 30-40 min after termination thereof. Visual analyzer function was evaluated according to the parameter of critical flicker fusion frequency (CFFF), which characterized the level of lability of the main nervous processes in the central element of this analyzer. Complex conditioned reflex activity was assessed according to accuracy of reactions to a moving object (RMO). The capacity for fine coordination of movements was tested by means of static tremometry (ST). Articulomuscular sensibility was evaluated according to capacity to reproduce a specified muscular exertion (RME). All measurements were taken using a PINR-03 instrument [5]. The data were submitted to statistical processing using the criteria of Student.

Results and Discussion

In the base state, differences in CFFF indices were noted in the different age groups. With increase in age, there was a reliable decrease in pilots of the test and control groups. There was a particularly significant change in the age group of 45 years and older, which is indicative of decreased functional ability of the main nervous processes in the central element of the visual analyzer, due to age-related changes. This is confirmed by deterioration of main visual functions in pilots over 45 years of age [6]. Consistent age-related differences in the base state were not demonstrable in the two groups of pilots with regard to other parameters.

Postflight testing revealed specific changes in the parameters studied among the Yak-40 pilots, although they were unrelated to age. Conversely, among helicopter pilots, there were reliable changes in all parameters for the group as a whole and consistent differences in different age groups.

Since the base data were different for different age groups, the results of postflight tests were submitted as percentages of the base levels.

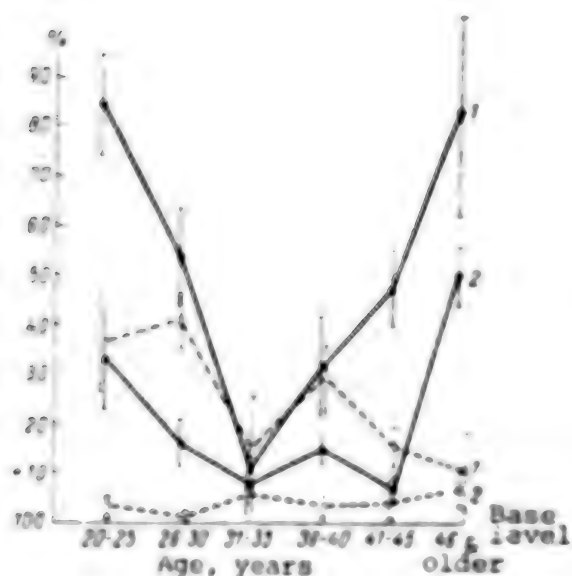


Figure 1.

Changes in RME (1) and ST (2) indices after flight in helicopter (solid line) and Yak-40 aircraft pilots (dash line) in different age groups

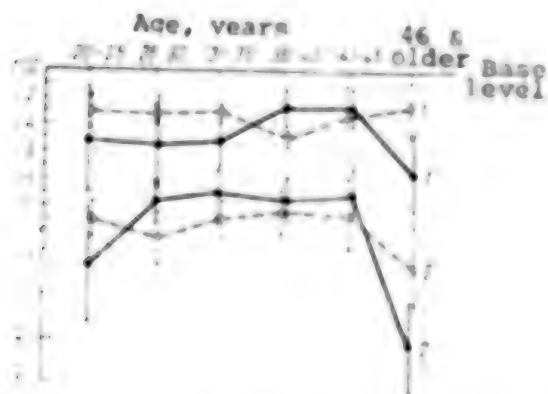


Figure 2.

Changes in CFFF (1) and RMO (2) indices after flight in helicopter (solid line) and Yak-40 aircraft pilots (dash line) in different age groups

Worsening of RME precision and elevation of ST after the flight were the most marked in the 20-25 year group (Figure 1); there was a reliable decline of CFFF and RMO (Figure 2). With increase in age the postflight changes diminished. The least changes in parameters were noted in the age range of 31-45 years. In the older age group, there was drastic increase in post-flight changes in psychophysiological indices.

Thus, in individuals 20-25 years of age, helicopter flights for a 7-h work day induced marked changes in higher nervous activity, functions of visual and motor analyzers. In the older age groups, the severity of these changes gradually diminished; however, in those over 46 years old they again became more marked. Evidently, the differences in parameters of different age groups are based on adaptive phenomena due to age-related psychophysiological distinctions. It is known that the degree of adaptation to various conditions is determined by the duration and frequency of man's exposure to them. Obviously, at a younger age with briefer work tenure and, consequently, insufficiently high level of occupational training, there would be poorer adaptation to helicopter flying conditions than at an older age. For this reason, there is faster development of signs of disintegration of psychophysiological functions in the course of a work day among individuals in the youngest age group. With increase in age and tenure, there is refinement of adaptive mechanisms and professional skills, which is associated with

attenuation of psychophysiological reactions to flight factors. In this respect, 45 years is apparently the critical age, since after this there is depletion of adaptive capabilities of the organism, which is the cause of drastic intensification of reactions to flight factors.

Vibration and noise are the prime factors in helicopter flights. The vibrations of modern Soviet helicopters are in the low- and medium-frequency ranges of the spectrum, and they could induce significant physiological changes in pilots [3, 4]. The noise in helicopter cabins also reaches significant levels that can have an adverse effect on man [7].

Apparently, it is expressly the effect of the vibration and noise factor, against the background of nervous and emotional stress, that led to development of the above changes. Among helicopter pilots as a group, these changes consist of a wide range of physiological effects of vibration and noise, which were of a reflex nature in this case. Moreover, we cannot rule out the direct effect of vibration on some organ or other, as a result of development of resonance phenomena [8-11].

The observed distinctions of psychophysiological changes in different age groups could also be related to the effects of the vibration and noise factor.

Many authors have reported that man adapts to vibrations and noise as time of contact with these factors increases. On the other hand, it has been demonstrated that the rate of development and severity of pathology related to vibration and noise depend on the age at which an individual starts to work under vibration-prone conditions [12, 13].

Our observations revealed that adaptation to the noise and vibration factor increases with increase in age and work tenure. However, at over 45 years of age, adaptive mechanisms are apparently depleted, and the body reacts with more significant changes to vibration and noise. This conclusion is consistent with the clinical data on changes in health status of pilots over 45 years of age [6].

Consequently, the greatest changes in psychophysiological functions after flying on helicopters were observed in pilots 20-25 and over 45 years of age. In the age range of 31-45 years, there were the least marked reactions to vibration and noise. The obtained data may be used in medical certification of flight personnel in the helicopter aviation.

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DIETARY SUPPLEMENTS USED TO PREVENT SOME CHANGES IN THE HUMAN BODY IN THE PRESENCE OF NERVOUS AND EMOTIONAL STRESS

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[Article by V. P. Bychkov and M. V. Markaryan, submitted 6 Sep 77]

[English abstract from source]

Simulated stress conditions (rise to a simulated altitude of 8000 m, anticipation of an emergency evacuation, mental work to be done under the conditions of time deficiency) brought about changes in the protein, carbohydrate, vitamin metabolism, heart rate, arterial tension, and peripheral blood. Nutrient ingredients (vitamins, glucose, minerals, processed concentrate) added to the diet before and during stress prevented or reduced the changes of the parameters studied.

[Text] Our objective was to investigate the condition of the body's internal environment in the presence of simulated stress situations similar to the occupational activities of cosmonauts, and to test under analogous conditions foodstuffs and elements that enhance adaptational capabilities of the body.

Methods

We conducted two 60-day studies with the participation of 10 healthy men ranging in age from 23 to 41 years (5 in each study).

Neuroemotional stress was induced by three models of stress situations. In the first, simulation of ascent to an altitude of 8000 m in a pressure chamber was used as a stressor; in the second, anticipation of gravitational accelerations on a centrifuge and in the third, performance of specified mental activity within an excessively short period of time under conditions of "success" and "failure" situations. Before each test, the subjects were informed at 1200 h about the test to be performed on the following day. Simulation of "ascent" was made by means of creating the appropriate noises in a GBA-63 pressure chamber, in which there was an altimeter connected to a vacuum pump, which enabled the subjects to see the "altitude" at which they were. During the test, we recorded the heart

and respiration rates. Prior to the second stress situation, the subjects were informed that they would be rotated on a centrifuge at accelerations of up to 8 G, and at 1100 hours the following day this factor was cancelled.

In the third stress situation, the subjects were allowed to choose among tasks varying in difficulty, each of which included working with cryptographic symbols for time and solving logic problems (G. Ayzenko's numerical test). This test was conducted by means of verbal instructions given by the investigator, and along with the reaction it permitted evaluation of intellectual distinctions of the subjects.

Before and after exposure to stress factors, we analyzed peripheral blood for amylase activity, sugar content, hemoglobin, erythrocytes, reticulocytes, thrombocytes, leukocytes and the leukocyte formula. In venous blood, we assayed total protein and protein fractions, free amino acids, cholesterol, total lipids, α - and β -lipoproteins, 11-hydroxycorticosteroids and aldolase activity. Total nitrogen, urea, amino nitrogen, uric acid, creatinine, epinephrine, norepinephrine, 17-hydroxycorticosteroids and vitamin C were assayed in 24-h urine samples.

In the second study, we tested three variants of food supplements, which included vitamins, minerals, glucose and phosphatide concentrate in different combinations, to correct changes in metabolic processes and physiological functions observed in the stress situations. The choice of these constituents was based both on their role in metabolic processes and information in the literature concerning a greater requirement for them in the presence of physiological tension [1-3]. The subjects took the food supplements for 5 days before modeling the stress situations and on the day of exposure to them (a total of 6 days).

The subjects were given the complete set of food supplements before "climbing to high altitude": 1 Undevit multiple vitamin lozenge, 180 mg ascorbic acid, 200 mg pangamic acid, 60 g glucose, 1.1 g potassium, 34 mg magnesium, 305 mg phosphorus, 1 g chloride, 300 mg calcium; prior to anticipation of rotation on the centrifuge, the subjects received all of these supplements, with the exception of vitamins; prior to the psychological test, they were given 1 Undevit multiple vitamin lozenge, 180 mg ascorbic acid, 60 g glucose and 80 mg phosphorus.

The diet of the subjects consisted of a ration of canned and dehydrated foods totaling about 2900 kcal in value. It contained about 140 g protein, 95 g fat and 350 g carbohydrates. In addition to this ration, the subjects took 2 Undevit multiple vitamin lozenges daily.

Results and Discussion

Simulation of an ascent (first study) induced an increase in blood serum total protein concentration in four subjects (mainly referable to albumins and γ -globulin fraction) and statistically reliable decrease in all tested

amino acids in most subjects. Anticipation of the centrifuge rotation led to a decline of 6 out of the 15 tested amino acids (valine, phenylalanine, tyrosine, cystine, proline, alanine). Evidently, these changes were related to increased utilization of amino acids for synthesis of albumins, as being the most labile proteins, and processes of gluconeogenesis. Conversely, the psychological test led to an increase in amino acid content, particularly glutamic acid with glutamine, the concentration of which tripled, which is apparently related to intensive glutamic acid metabolism in the brain, and it was associated with accumulation thereof in blood plasma [4].

A decrease in daily excretion of total nitrogen in urine was observed in most subjects under the influence of the "climb." On the day of exposure, total nitrogen excretion constituted a mean of 13.7 g/day, versus 16.3 g in the background period. On the following day, there was generally no change in excretion of total nitrogen (13.7 g/day). Only 1 day after being in the pressure chamber did we obtained values close to background levels. Anticipation of rotation on the centrifuge led to some decline of total nitrogen in three subjects. During the aftereffect period, we observed an increase in total nitrogen content of 24-h urine to a mean of 18 g in all of the subjects.

Analysis of the results of testing the glycemia level revealed that there was an increase in sugar concentration in blood of 2 subjects under the influence of the pressure chamber, while anticipation of centrifugation elicited elevation of this index in all subjects (a mean of 69-94 mg%). In the background psychological studies, the glycemia level was higher than with exposure to a real psychological factor (107 mg%, versus 76 mg%). These data indicate that emotional factors induce primarily a hyperglycemic response.

The results of our studies failed to demonstrate appreciable changes in concentration of cholesterol, total lipids, α - and β -lipoproteins. This could be attributed either to the fact that the stressors were not strong enough and did not affect metabolism, or else that the blood tests were made at long intervals, for which reason we could not detect the changes. Our assumption is confirmed by several studies [5, 6], which demonstrated that the blood cholesterol content may increase very rapidly under the influence of stress, but then it may also decrease rapidly.

Studies of vitamin metabolism demonstrated a significant decrease in excretion of ascorbic acid in 24-h urine in the background tests and real studies with the psychological test (40 mg, versus 87 mg in the background). These findings indicate that the vitamin C requirements of the body are increased in the presence of stress [7, 8].

The pulse rate record during the period of "ascent" revealed that it became faster in three out of four subjects. After "descending to earth," their pulse remained 7-19/min faster than background levels. There was no change in respiratory rate. Some subjects reported subjective sensations, in the form of stuffed and painful ears.

Examination of peripheral blood revealed that the most marked blood changes were observed in response to anticipation of rotation on the centrifuge. Thus, in blood taken from three subjects just prior to the stress factor we found an increase in leukocytes, segmented neutrophils and decrease in relative lymphocyte content (up to 18%). The reaction of the blood system to the pressure chamber was referable mainly to the leukocyte formula: relative lymphocyte count dropped from 40-47 to 20% in 2 subjects, and in 1 case it dropped to 11% (versus 30% in the background period) immediately after the pressure chamber. On the 2d day of the aftereffect period, there was a tendency toward return of this parameter to background levels. We failed to demonstrate appreciable changes in the rest of the hematological indices.

As a result of testing the functional state of the adrenals, we found an increase in daily excretion of 17-hydroxycorticosteroids in urine due to simulated ascent and anticipation of centrifuge, which is indicative of increased adrenocortical function. Excretion of epinephrine and norepinephrine remained unchanged.

In the second study, there was only a tendency toward increase in blood serum albumins under the influence of the pressure chamber, against the background of food supplements. The food supplements, and particular the complex thereof, had a corrective effect on amino acid composition of blood plasma. Thus, under the influence of the "ascent" there was a decrease in concentration of only some amino acids (valine, proline, alanine, glutamic acid with glutamine); anticipation of rotation on the centrifuge induced a decrease in glutamic acid with glutamine, while the psychological test did not elicit appreciable changes in amino acid content of blood plasma.

The food supplements had a beneficial effect on nitrogen metabolism in the first and second stress situations. A tendency toward decreased excretion of total nitrogen was only observed during performance of the psychological test, when urea content of urine decreased, while amino nitrogen increased, which is apparently attributable to the lesser participation of amino acids in the process of gluconeogenesis as a result of including glucose in the food supplements.

The food supplements did not affect regulation of glycemia in the "ascent" situation. Prior to this, all subjects presented an increase in blood sugar concentration, which constituted a mean of 107 mg%, versus 72 mg% in the background period. As in the first study, there was an appreciable elevation of glycemia level prior to the background psychological test. A beneficial result was demonstrated when glucose was used in combination with minerals and phosphate concentrate in the situation of anticipation of centrifuge rotation.

We failed to demonstrate substantial changes in excretion of ascorbic acid, which is indicative of saturation of the body with vitamin C.

A faster pulse was found in only one subject during the "ascent." This was not associated with any subjective sensations.

The results of the second study also revealed that, against the background of using food supplements, there was merely an increase in leukocyte count, with no change in leukocyte formula, under the influence of the pressure chamber and anticipation of centrifuge rotation. Moreover, we demonstrated some intensification of adrenocortical function during simulation of ascent.

Thus, changes were obtained in protein and carbohydrate metabolism, vitamin C metabolism, morphological composition of peripheral blood, adrenocortical function and heart rate as a result of reproducing stress states.

We observed considerable individual fluctuations of degree of manifestation of the above reactions, and this is apparently related to the subject's type of higher nervous activity.

It was demonstrated that the food constituents (vitamins, minerals, glucose, phosphatide concentrate) used in our studies as supplements on the eve and during the period of stress situations prevented a number of changes that the stressors induce in the subjects. The corrective influence of the food supplements was manifested by absence of changes in protein composition of blood serum, vitamin C metabolism, morphological composition of peripheral blood and heart rate.

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ROENTGENOLOGICAL EXAMINATION OF THE HUMAN HEART AFTER 100-DAY HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 28-31

[Article by I. G. Krasnykh, submitted 15 Nov 77]

[English abstract from source]

Two groups of male test subjects (each of 3 persons) took part in a 100-day bed rest experiment. During the study Group 2 did exercises. X-ray examinations showed that bed rest induced changes in the roentgenoanatomical structure of the heart, a decrease of its contractile function. In Group 2 these changes were far less pronounced. The recovery took 3 to 6 months.

[Text] The increase in incidence of cardiovascular diseases is related to the decrease in share of physical labor in modern man's activities [1]. Hence, it is understandable that increased interest is displayed in the problem of hypokinesia, which is acquiring social significance. In this investigation, we used x-ray methods to examine the effect of 100-day hypokinesia on the size of the heart and its contractile function; we assessed the efficacy of complex physical conditioning, and we monitored the process of restoration of roentgenological characteristics of the heart.

Methods

We studied two groups of male volunteers 21-22 years of age, who maintained strict bed rest for 100 days. The first group of subjects (N-ev, N-ov, K-v) performed only the most necessary movements, while the second group (L-ch, Yu-n, M-o) regularly performed a set of special exercises in supine position. On the 99th day, i.e., just prior to terminating bed rest, they took pharmacological stimulants. The volume of the heart in systole and diastole, as well as stroke volume, were calculated on teleroentgenokymograms [2-5]. We determined the cardiac coefficient as the ratio of heart volume to body weight. Myocardial contractility was assessed from the structure of the notches on the lateral outlines of the roentgenokymograms. Pilot x-rays of the chest and anterior teleroentgenokymograms of the heart were taken with the subjects standing. We tried to recreate identical conditions for all tests and background studies.

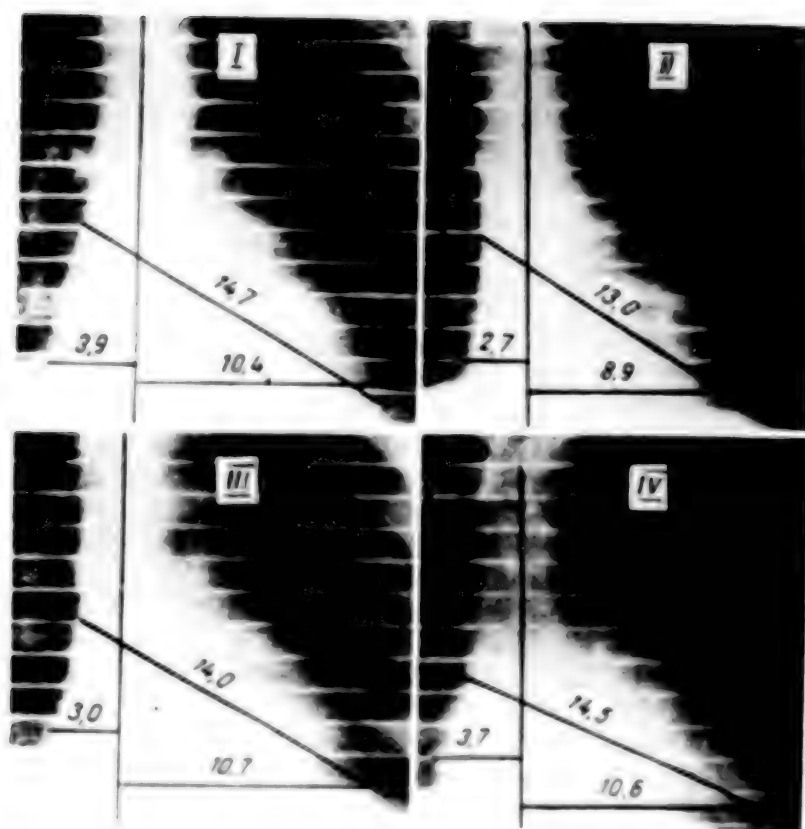
Changes in heart size and cardiac coefficient after 100-day hypokinesia

Group of subj.	Time of examination	Heart volume, cm ³		Cardiac coef- ficient
		systole	diastole	
1st	Background	712-996 816	838-1215 969	12.7
	Immediately after hypokinesia	511-732 625 (-23.3%)	580-832 708 (-26.9%)	9.8 (-22.8%)
	1 month after hypokinesia	592-810 684 (-16.1%)	703-997 822 (-15.2%)	11 (-13.3%)
	3 months after hypokinesia	657-928 793 (-8.8%)	755-1062 906 (-12.5%)	12 (-5.5%)
2d	Background	744-898 825	889-1044 963	13.7
	Immediately after hypokinesia	692-774 734 (-11.0%)	820-881 852 (-11.5%)	12.3 (-10.2%)
	1 month after hypokinesia	711-830 776 (-5.9%)	846-948 900 (-6.6%)	13.0 (-5.1%)
	3 months after hypokinesia	735-832 796 (-3.5%)	879-988 908 (-2.7%)	13.5 (-1.5%)

Note: Extreme values are given in the numerator and mean values in the denominator. Relative changes in comparison with base indices are given in parentheses.

Results and Discussion

On the first few days after bed rest, all of the subjects complained of general weakness, increased fatigability, palpitations, pain in joints and muscles of the lower extremities and instability when walking. These disturbances were considerably more marked in the first group of subjects. The Table lists the results of determining heart volume and cardiac coefficient in both groups of subjects. In the first group, heart volume in systole and diastole decreased by a mean of 24 and 26%, respectively, in the course of 100-day hypokinesia (by 14 and 13% in N-ev, 27 and 32% in K-v, by 31 and 32% in N-v). Estimation of systolic ejection of blood revealed that this index was 3% lower than the background level (the individual decline ranged from 20 to 50%). The cardiac coefficient was 23% lower than in the background examination.



Anterior teleroentgenokymograms of the heart of subject N-v

I) background

II) immediately after hypokinesia

III & IV) 3 and 6 months, respectively, after hypokinesia

The figures indicate the main dimensions of the heart. The size of the heart, height of notches along left and right outline, as well as number thereof on roentgenokymogram strips were restored only 6 months after hypokinesia.

Comparative analysis of serial pilot roentgenograms of the chest and teleroentgenokymograms of the heart revealed a decreased in roentgenoanatomical size of the heart shadow and change in its shape (see Figure). Immediately after hypokinesia, we observed an appreciable reduction of both the right (indicative of decreased venous return) and left heart (confirming the

estimated decrease in stroke volume). The changes in size and shape of the heart were associated with signs of change in myocardial contractility. The amplitude of left ventricular notches was reduced to one-half to one-third [the base value], while the number thereof more than doubled in each band of the roentgenokymogram. The significant reduction of notches against the background of tachycardia could be indicative of diminished myocardial contractility and force of cardiac contractions [2, 3, 6]. The rehabilitation period was quite long. Heart volume in systole and diastole as an average of 16 and 15% smaller, respectively, 1 month after hypokinesia. Stroke volume was 10% decreased and the cardiac coefficient was 13% lower. In one subject, the dimensions of the heart and myocardial contractility reverted to normal after 3 months and in two this occurred after 6 months.

In the second group of subjects (L-ch, Yu-n, M-O), the changes in heart volume on the last day of hypokinesia were 2-2.5 times less marked than in the first group, stroke volume was almost 3 times less marked. There was faster recovery, and the parameters studied virtually reached base levels by the end of the 3d month. Thus, the obtained data show that 100-day hypokinesia induces significant changes in roentgenoanatomical structure of the heart, with about 25% decrease in its volume, as compared to the base figure. The reduction of heart volume is associated with decreased myocardial contractility.

The changes in heart size in the course of man's vital functions is determined primarily by the change in filling with blood of the entire heart or its different cavities, then by increase or decrease in weight of the myocardium [3, 7-9]. Apparently, the decrease in heart volume during hypokinesia is due both to decrease in delivery of blood and myocardial weight loss. The studies of several authors [9-14] demonstrated that bed rest leads to loss of plasma, reduction of systolic and minute volume of the heart. Our data confirmed these findings. The decrease in size of the right and left heart on the roentgenokymograms is indicative of diminished return of blood to the right heart and systolic ejection. At the same time, in experiments on rats, a decrease in heart weight was found after 120-day hypokinesia [11]. The longer rehabilitation period with normalized hemodynamics is indirectly indicative of myocardial weight loss. Evidently, diminished myocardial contractility is the consequence of effects of many factors, including changes in metabolic processes in the myocardium as a result of neurohumoral and circulatory disturbances [9, 11, 12, 13].

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EFFECT OF SPACE FLIGHT CONDITIONS ON DEOXYRIBONUCLEOPROTEIN AND NUCLEIC ACID CONTENT OF RAT TISSUES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 32-35

[Article by E. Misurova, R. A. Tigranyan, K. Kropacheva and M. Praslicka,* submitted 16 Jan 78]

[English abstract from source]

The spleen of rats flown for 19.5 days aboard the biosatellite Cosmos 782 showed a significant increase in polydeoxyribonucleotides and a decrease of DNP and DNA. The spleen of synchronous rats did not exhibit any differences. This suggests that the increase in polydeoxyribonucleotides in flight rats immediately post-flight was a result of the increased gravity stress. The liver and white blood cells did not display any significant changes in DNP or nucleic acids. The changes in the content of nucleic acids in the thymus and bone marrow were insignificant.

[Text] Exposure to some physicochemical factors (ionizing radiation, alkylating compounds, glucocorticoids) is associated with impairment of deoxyribonucleoprotein (DNP) of lymphatic and hemopoietic tissues, which is manifested by increased solubility of DNP in saline [1-4]. The soluble fraction consists of polydeoxyribonucleotides (PDRN), the level of which rises starting in the 2d h after exposure, with a maximum at the 4th-8th h; however, in time (mainly by the end of the 1st 24 h), the PDRN level reverts to normal [5-7]. Since elevation of level of soluble PDRN is related to pyknosis and death of cells, there is gradual decrease in DNP content of tissues.

Our objective here was to investigate the effect of space flight factors on DNP in the rat spleen and liver, amount of nucleic acids in the spleen, thymus, bone marrow, liver and leukocyte mass of rat blood.

Methods

We conducted our studies on male Wistar-SPF rats 6-10 h and 26 days after completion of a 19.5-day space experiment aboard the Cosmos-782 biosatellite. The obtained data were compared to the results of studies of animals in a synchronous experiment and Vivarium control.

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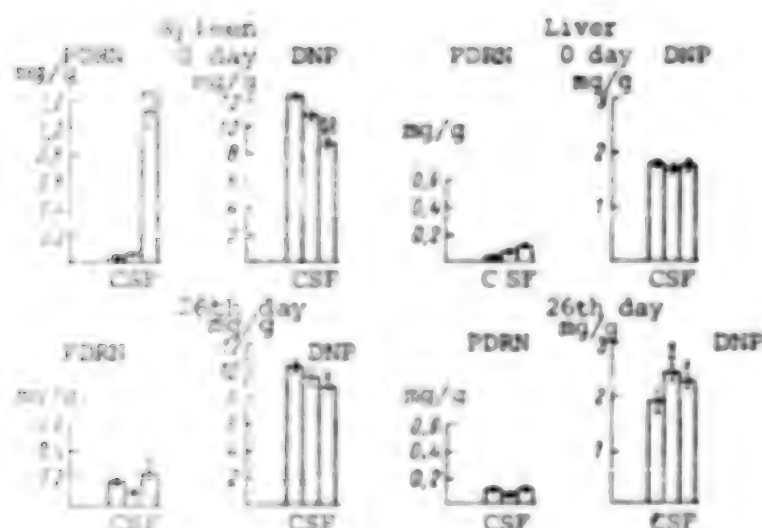


Figure 1. PDRN and DNP concentration in the spleen and liver.

here and in Figure 2, the following applies:

Results for 6 animals are given (M \pm m). Statistical reliability in relation to control group: X) $P < 0.05$, XX) $P < 0.01$; in relation to synchronous group: α) $P < 0.05$, $\alpha\alpha$) $P < 0.01$.

C) - control S) - synchronous experiment F) flight

We assessed DNP changes on the basis of assaying its concentration in tissues and levels of soluble PDRN [1]; PDRN in the soluble fraction and DNP in the insoluble fraction were expressed in milligrams DNA per gram wet tissue.

Nucleic acids were assayed by the method of Tsanev and Markov [10], expressed in milligrams P/100 g wet tissue (concentration) and milligrams P/organ (total content). The obtained data were submitted to processing by means of analysis of variation and the Duncan test.

Results and Discussion

Studies of DNP level revealed that the most significant changes were found in the spleen. In the flight group of animals, the PDRN level increased by almost 80 times immediately after landing (Figure 1). The elevation of PDRN level is indicative of impairment of DNP of part of the cells, and it is related to a 25% decrease in concentration of DNP, as compared to control levels (Figure 1). The PDRN level in the spleen did not differ from the control 24 days after the flight; however, the concentration of DNP was still lower than in control animals. No changes in DNP concentration were demonstrated in the synchronous experiment.

Immediately after landing no changes were noted in DNP concentration in the liver; however, 26 days after termination of the experiment, there was moderate increase in concentration of DNP in the liver of rats in both experimental groups (see Figure 1).

RNA content of the spleen of flight rats was reduced to one-third, as compared to the control, 6-10 h and 26 days after landing. In the animals in the synchronous experiment, we demonstrated a decrease in concentration and total RNA content only at the first examination (Figure 2a). DNA concentration in the spleen was moderately decreased immediately after landing, while total DNA content was decreased to almost one-half; there was partial restoration of DNA content 26 days after the flight, while DNA concentration did not differ from that of control animals. No changes in DNA content of the liver were demonstrated in the synchronous experiment (Figure 2a).

Concentration and amount of RNA in the thymus of the flight group of rats were diminished only immediately after landing; DNA concentration did not change in these animals; however, at both tested times, total DNA content was 20% lower than control levels. In the synchronous experiment, nucleic acid content of the thymus did not differ from that of intact animals (Figure 2b). No changes were demonstrated in nucleic acid content of the liver, with the exception of an increase in concentration of RNA in animals in the flight and synchronous groups 26 days after termination of the experiment.

There were negligible changes in nucleic acid content in bone marrow of flight animals, and none in the synchronous experiment (Figure 2c).

Changes in nucleic acid content of blood leukocytes were observed only in rats in the synchronous experiment. In these animals, the RNA concentration decreased 6-10 h after landing, with total restoration thereof after 26 days, and concurrent increase in concentration of DNA (see Figure 3).

The submitted data indicate that space flight factors induce the most severe changes in the spleen. Elevation of PDRN level after landing (after 6-10 h) is indicative of impairment of DNP at the last stages of the space flight. This assumption is based chiefly on the following facts: 1) elevation of PDRN level is a nonspecific reaction of hemopoietic and lymphatic tissues to various factors that induce pyknosis and death of sensitive cells (for example, ionizing radiation, cytostatic agents, glucocorticoids, formalin) [1, 3, 4]; 2) the PDRN level rises already in the 2d h after exposure and reaches a maximum after 4-6 h. Since the formed PDRN are dissociated in tissues and eliminated in blood [2], the level thereof in tissue drops rapidly and reaches normal within a day. According to the foregoing, a high PDRN level is observed 4-15 h after termination of exposure to the deleterious factor; 3) since no changes in this index occurred in the spleen of rats in the synchronous experiment, it may be assumed that elevation of PDRN level in the flight group of rats after landing (after 6-10 h) is the result of so-called gravitational stress.

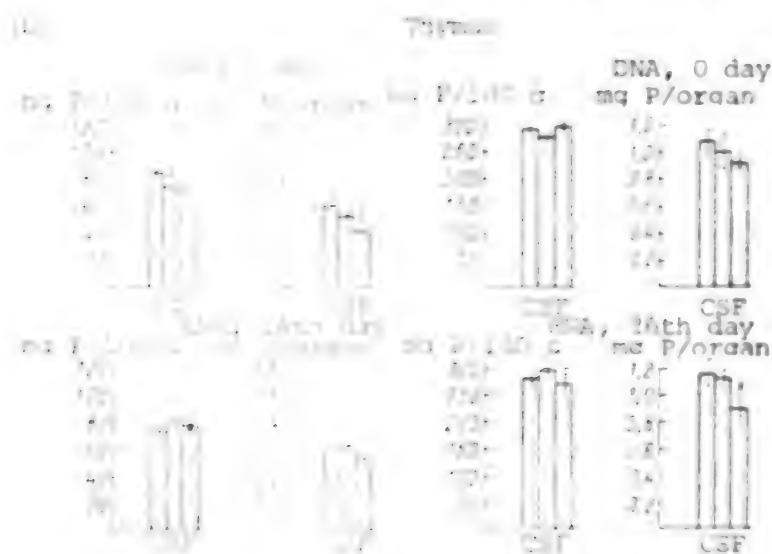
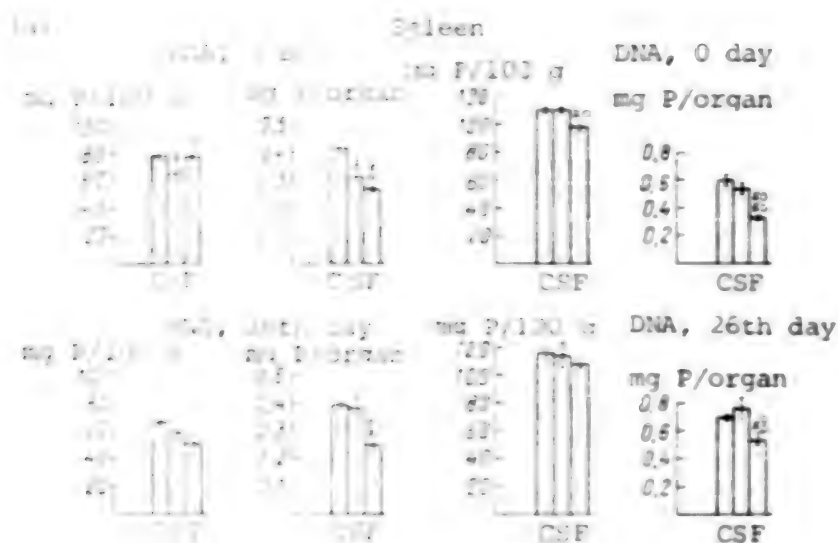


Figure 2.
Concentration and
total RNA and DNA
content in the spleen
(a), thymus (b), bone
marrow (c) and blood
leukocytes (d)

Concurrently with elevation of PDRN level, there was a decrease in concentration of DNP and DNA in the spleen of flight rats, which is indicative of removal of part of the cells with high nucleocytoplasm ratio, namely, the lymphocytes, whose DNP is the main source of PDRN [2].

The data pertaining to DNA content, the levels of which may be considered as a biochemical indicator of cellularity of organs [11, 8], are indicative of significant damage to the spleen, and there was only partial recovery thereof within 26 days. Interestingly enough, the changes in amount of nucleic acids in the thymus and bone marrow were less overt than in the spleen. No substantial impairment of DNP or nucleic acid content was demonstrated in the liver and blood leukocytes.

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REACTIONS OF THE THERMOREGULATORY SYSTEM FOLLOWING PROLONGED HYPOKINESIA

RUSSIAN JOURNAL OF ANATOMICAL BIOLOGY AND AVIATION MEDICINE in Russian No 5, 1979 pp 55-62.

[Article by T. V. Vasil'yev, G. D. Glod, Ye. P. Mel'nikova, L. N. Nikol'skiy, S. V. Petrovskiy, S. I. Gynik and N. N. Uglova, submitted 7 Apr 78]

(English abstract from source)

The authors studied the thermoregulatory system of white rats of the 1st generation of hypodynamic rats and the 2nd generation of hypodynamic rats after 30 day hypokinesia. The results of the study show that the thermoregulatory system of the 2nd generation of hypodynamic rats approached the initial level.

[Text] The authors have demonstrated that several systems and dystrophic changes in different organs and tissues have been demonstrated as a result of analysis of experimental material dealing with general and special aspects of the effects of long-term hypokinesia on the organism [1-8]. Thus, substantial changes have been noted (including prolonged hypokinesia in the nervous, endocrine and cardiovascular systems [1, 9-11]). Hypokinesia also has an adverse effect on general and immunological reactivity of the organism [12, 13].

[Text] The authors have also noted the distinctions of development of shock, hemorrhage, and other pathological processes against the background of hypokinesia [14]. The authors have concluded that other pathological processes may also develop typical deviations against the background of hypokinesia.

[Text] The authors have made an attempt to clarify the influence of hypokinesia on the development of hyperthermia and dynamics of the thermoregulatory system of the animal thermoregulatory system.

Methods

[Text] The authors studied the thermoregulatory system of 30 white rats weighing 150-200 g. In the 1st generation of hypodynamic rats the distinctions of reactions to overheating

(40 min) and state of the organism in the recovery period (350 rats); in the second series, we determined the compensatory capabilities of the thermoregulatory system by overheating the animals until they died (170 rats). In both series of studies, the rats were submitted to heat on the 1st, 3d and 7th days after hypokinesia.

Hyperthermia was produced concurrently in 2 experimental and 2 control rats in a 1.5-m³ incubator at a temperature of 40-42° and relative humidity of 35-45%. The animals were placed in special box-cages that permitted recording of physiological parameters. To produce 15-day and 30-day hypokinesia, the rats were kept in special cages that allowed us to reliably restrict their movements but not intake of feed, water and elimination. The temperature was held at 18-20° in the room where they were kept. During the period of hypokinesia, we conducted general clinical observations and monitored the weight of the animals.

Reaction to overheating was evaluated by the change in rectal temperature, heart and respiration rate; in some experiments, we used the results of EKG, EMG of lumbar muscles, as well as results of pathomorphological studies. In addition, we determined fluid loss in some animals, according to difference between weight before and after hyperthermia. Copper-constantan thermocouples were used to measure temperature and records were made on an automatically recording Graffipot galvanometer with accuracy to $\pm 0.05^{\circ}\text{C}$. Respiratory excursions of the chest (carbon-powder sensor) and EKG were recorded on an electroencephalograph, and the EMG on a 42V myograph. The obtained results were submitted to statistical analysis.

Results and Discussion

The animals tolerated restriction satisfactorily. Overheating after 15 days of hypokinesia demonstrated changes in reactivity of the rats' thermoregulatory system. Extension of hypokinesia from 15 to 30 days did not affect the nature of these changes, but they became less marked.

The rats behaved similarly after being placed in the heat chamber. For the first few minutes, we observed the usual orienting reaction; then the animals quieted down, but by the 20th-30th min they again began to display restlessness in the form of increases of increased motor activity. At first these increases alternated with periods of adynamia, then were replaced by the latter. This was associated with marked dyspnea. The animals usually died presenting signs of fading of cardiac activity. Tonic-clonic seizures were observed in the terminal period in some animals, mainly controls.

From the first moment of overheating, rectal temperature began to rise in all rats at about the same rate (Figure 1). By the 40th min of exposure, the temperature increased, on average, $2.0 \pm 0.2^{\circ}\text{C}$.

In the first series of experiments, there was simultaneous restoration of rectal temperature in all experimental rats. In control animals, this

process was a mean of 12 min behind, and by the time their temperature was restored (40th min of aftereffect period), it was already 0.5–0.8°C below the base level in experimental animals. It may be assumed that the temperature drop is the result of hypercompensatory reaction to heat in rats submitted to hypodynamia.

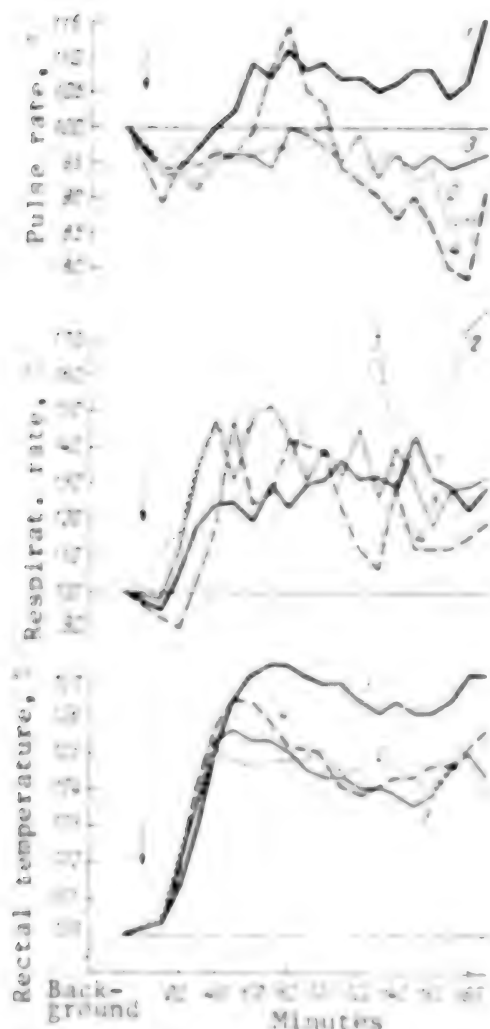


Figure 1.
Dynamics of physiological parameters (% base level) of rats during overheating after 15-day hypokinesia. Arrow shows start of overheating.

1) control
2, 3, 4) 1st, 3d and 7th days,
respectively, of
readaptation

In the second series of studies, where the rats were left in the heat chamber until they died, rectal temperature continued to rise. In the control, the maximum temperature increment constituted 2.9°C and it was recorded on the average in the 65th min of exposure. The temperature held at the attained level (41.4–41.6°C) for a long time, and abruptly rose to $43.3 \pm 0.34^\circ\text{C}$ only 20–30 min before death.

In all hypokinetic rats in the second series of studies, overheating induced a reliably less marked temperature elevation (to 40.4–41.2°C); however, death of these animals occurred at about the same body temperature as in control animals (43.1°C).

Analysis of the data on dynamics of cardiac activity (see Figure 1) indicates that acute overheating was associated with a decrease in heart rate. This somewhat unusually reaction was apparently attributable to the relatively high base level of this parameter (452–478 beats/min) in view of immobilization of the animals. By the 40th min of exposure, this parameter was restored to the base level only in control rats. About 15 min after discontinuing heating, the heart rate of virtually all animals was close to the background level. The only exception was referable to rats submitted to heat on the 1st day of readaptation; even in the presence of restored rectal temperature, their heart rate continued to decline and constituted 84.7% of the base level.

In the second series of studies, we failed to demonstrate substantial differences between control and experimental animals, with respect to dynamics of heart and respiration rate (see Figure 1).

Survival time after overheating control animals constituted 160 ± 13 min, with 100% mortality. At the same time, of the rats kept under hypokinetic conditions and overheated on the 1st, 3d and 7th days of readaptation, 54.5, 62.5 and 83.3% expired at the following mean times: 217 ± 26 , 295 ± 23 and 226 ± 46 th min ($P < 0.05$), respectively (Figure 2). In all cases, the experimental rats were more resistant to high temperature.

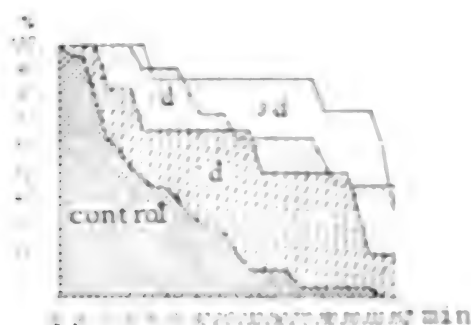


Figure 2.

Survival of rats overheated on the 1st, 3d and 7th days after 15-day hypokinesia

However, the differences from background levels were found to be statistically unreliable in both cases (with respect to quantitative expression).

Evaluation of animal resistance to heat loads according to weight loss revealed that relative weight loss due to loss of fluid during overheating was more marked in all rats submitted to hypokinesia. Thus, while this index constituted 2.5% of base weight in control animals, it constituted 3% on the 1st readaptation day, 3.6% on the 3d and 3.8% on the 7th day ($P < 0.05$).

Analysis of the EMG led to the conclusion that overheating reduced electrical activity of muscles, in both the experiment and control.

The results of the morphological studies are of considerable interest: In the myocardium of control rats we observed signs of reduction of level of biological oxidation processes (decreased glycogen content of cardiomyocyte sarcoplasm, decreased succinate dehydrogenase and NAD activity) and an increase in intensity of energy production due to glycolysis and oxidation of lipids and amino acids (increased activity of lactate dehydrogenase, β -oxybutyrate and glutamate) after overheating. When the animals were overheated on the 1st day after 15 days of hypokinesia, which had already led to decreased activity of enzymatic processes involved in biological oxidation, there was further depression thereof, and it was more marked than in the control (Figure 3).

The findings were somewhat different after 30-day hypokinesia, when there were morphological signs of intensification of myocardial function. Against this background, overheating induced some normalization of structural manifestations of metabolism, and only lactate dehydrogenase activity remained elevated. Activity of enzymes related to processes of biosynthesis decreased to about the same extent in all animals. There was faster regression of changes in the myocardium of rats submitted to overheating after

hypokinesia than in control animals. By the 14th day of the recovery period they presented only higher activity of monoamine oxidase in the myocardium, which corresponded to the demonstrated morphological signs of increased catecholamine secretion in the adrenal medulla.



Figure 3. Decrease in succinate dehydrogenase activity in the rat myocardium after overheating (combined tissue block); objective 40 \times ; Homal VI.

A) control

B) 15-day hypokinesia

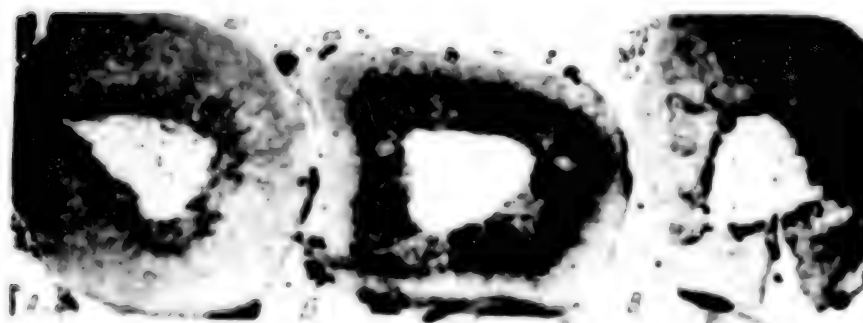


Figure 4. Dihydroorotate dehydrogenase activity in adrenal cortex of rat (combined tissue block).

A) control rats after overheating

B) 30th day of hypokinesia

C) 30th day of hypokinesia after overheating

without overheating

Varying degrees of morphological changes inherent in the "alarm stage"--central delipoidization, increased RNA content, increased activity of -oxybutyrate and dihydroorotate dehydrogenase--were observed on the 4th day after overheating in the adrenals of control rats and animals submitted to hypokinesia (Figure 4).

The initial state of the adrenal cortex was not the same prior to heating in intact and hypokinetic animals. The latter presented an increase in relative weight of the gland, a wide fascicular zone with many lipids in the cells and change in enzymatic activity, indicative of the state inherent in the "resistance stage." On the basis of the results of the morphological studies, it may be assumed that the reaction of the adrenals to overheating began with the "resistance stage" in animals submitted to hypokinesia.

On the basis of the results obtained, it can be concluded that restriction of movements for 15 and 30 days had a certain influence on the thermoregulatory system of albino rats, as a result of which their resistance to extreme heat loads increased.

Typically enough, overheating the experimental animals was associated with more marked deviations of the studied parameters from the base level (severity of dyspnea, fluid loss, change in cardiac activity, faster normalization of rectal temperature). Only body temperature increased more significantly during overheating in control rats than in animals submitted to hypokinesia.

A. Ya. Tizul [13] established that torpidity and hyporeactivity were the most common features of changes in thermoregulation in man during 120 days of hypokinesia. That this does not coincide with our findings can apparently be attributed both to differences in objects studied and methodological differences in assessing thermoregulation.

In the case of exposure to extremely high temperatures, the organism finds itself immediately under difficult conditions and has no spare time to promptly trigger compensatory mechanisms, particularly on the level of tissular processes that are capable of increasing resistance to heat more effectively. Obviously, under these conditions, organisms whose functional state was altered in advance and provided for higher resistance to hyperthermia will be more resistant.

We know from the literature [14, 15] that thermal hypoxemia is one of the elements in the genesis of disorders and death due to hyperthermia. Yet animal resistance to hypoxia increases under the influence of prolonged restriction of movements [16]. This effect can apparently be attributed to a decrease, under the influence of hypokinesia, in activity of enzymatic processes involved in biological oxidation, increased intensity of glycolysis, which in turn is manifested by more intensive decrease in heat production against the background of exogenous hyperthermia in animals submitted to hypokinesia. Consequently, it may be assumed that some increase in resistance to hypoxia is one of the causes of increased polyphysiologic resistance of animals to extreme heat loads.

Furthermore, we must not fail to bear in mind that hypokinetic rats were exposed to hyperthermia against the background of an already altered functional state of the adrenals, corresponding as we have mentioned above to the second stage of the adaptation syndrome, the "stage of resistance" [17]. This could also be one of the causes of increased survival of experimental rats at high ambient temperature.

It is interesting to assess the increased resistance of rats to hyperthermia following hypokinesia from the point of view of L. Kh. Garkavi et al. [18] concerning nonspecific conditioning reactions and activation at different levels of reactivity. In their opinion, repeated exposure to stimuli could lead to development of a reaction characterized by increase in active resistance.

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EFFECT OF HYPOKINESIA ON HIGHER NERVOUS ACTIVITY OF ALBINO RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 41-44

[Article by M. A. Kuznetsova and Ye. S. Meyzerov, submitted 14 Mar 77]

[English abstract from source]

The effect of a 22 day hypokinesia study on the labyrinthine behavior of white rats was investigated. The test animals showed certain behavioral changes which developed throughout 22 days. However, significant changes occurred only during the first 6-7 days. From the 8th day the changes diminished but retained their trend. It is believed that the behavioral changes are mainly associated with inhibition of the nervous processes of higher cerebral representations responsible for the higher nervous activity.

[Text] Restricted movement and lower level of muscular activity are significant factors that affect the body during a space flight. Prolonged inactivity of the skeletomuscular system induces development of the hypodynamia syndrome. The disturbances that appear extend to virtually all organs and systems, they create conditions for changes in metabolism and neurohumoral mechanisms of regulation of somatic and autonomic functions [1].

This problem is acquiring broad social significance with the development of industrial technology and mechanization, and this explains the systematic study thereof at the present time. However, there are few special studies of the effect of this factor on the central nervous system (CNS) and particularly on higher nervous activity (HNA). Among the sources available to us, we found only the work of L. N. Karuleva on the effect of hypokinesia on HNA of animals [2]. Most studies on this subject were conducted on people who spent a long time in bed. Either a change in afferent impulsion from the periphery or impairment of cerebral hemodynamics as a result of maintaining a horizontal position for a long time could have been the cause of the demonstrated disturbances in functional state of the CNS [3, 4].

Both mechanisms are also involved in space flights. In ground-based experiments on animals, it was established that the role of the latter mechanism is minor, since keeping the animals in small boxes for a long time did not alter the hydrostatic column of blood.

We submit here the results of studying HNA of albino rats during 22-day hypokinesia.

Methods

We used male Wistar rats in this study. We assessed the state of HNA according to the animals' ability to develop an algorithm of behavior in a maze with doors [5], as well as ability to use it in developing new habits in finding feed in the maze. During the experiment, the animals were put in the maze three times. We recorded the number of times they refused to go through the maze, time and number of mistakes made in crossing through it, as well as number of aberrant signs characterized by inadequate behavior of the animals during the experiment (persistent unwillingness to go through a door opened for them). In analyzing the data, we also took into consideration the dynamics of mistakes during the test. Monotonous decrease in number of mistakes from run to run was considered optimum dynamics. Any deviation from these dynamics was evaluated as a disturbance characterizing depletion of the nervous system. We estimated the percentage of these deviations, as well as number thereof, as compared to the preceding run. In one of the experiments, the number of runs into the maze was increased to 16, while the number of one-time food reinforcements was reduced accordingly, in order to avoid satiation.

Before the experiment, the animals were trained to find the feed compartment in the maze with unlocked but shut doors. The animals could pass into the next lane by pushing any door with their forehead. After they learned to do this, the animals were divided into two homogeneous groups, according to time required to reach the feed compartment (12 rats in each group). The first group of rats was kept in boxes for 22 days and the second group (5 per cent) in the vivarium. The HNA experiments were repeated on the day after the animals were removed from the boxes to their usual surroundings. Work began with restoration of the previously acquired skill in going through the maze with the doors unlocked but tightly shut. After the animals began to reach the feed compartment within no more than 40 s, some of the doors were locked and the animals successively developed three skills for finding feed in the maze with locked doors using a previously described method [5]. Development of the first skill began on the 2d-4th days after taking the animals out of the small boxes, the second on the 12th and the third on the 18th day. The experiment with an increased functional load was conducted on the 19th day.

The obtained data were submitted to processing according to criteria of comparison of two series of regression by quantitative and qualitative tags [6] and, in some cases, using the criterion of Student.

Results and Discussion

The studies revealed that the second groups of animals regained their skill in going through the maze with unlocked doors within a mean of 7.7 days; the first group of animals did so in 3.6 days ($P < 0.01$). This phenomenon was

apparently not related to the fact that 3 of the 12 experimental animals were in less than satisfactory condition (alopecia, lameness, listlessness) immediately after removal from the boxes, since there was no correlation between slower passage through the maze and the animals' condition.

When developing the first skill in the maze with locked doors, for the first 3 days the first group of animals presented reliably ($P \leq 0.05$) more refusals to go through the maze than the second group (Figure 1). There was appreciable screening of orientation in the new situation in the first group of rats. They went through the maze with locked doors making a greater ($P \leq 0.02$) number of mistakes (Figure 2) and spent more time on this ($P \leq 0.05$) than the animals in the second group. In other respects, the indices of development of the first skill coincided in the two groups of animals. Starting on the 2d day of development of the first skill, the first group of animals made reliably fewer mistakes than the second group (see Figure 2).



Figure 1.

Mean refusals (%) to go through maze with locked doors. Here and in Figure 2:

- 1) hypokinesia
- 2) control

X-axis, experiment No; y-axis, percentage of refusals

animals, since they consumed the feed offered them in the vivarium entirely and never refused additional feed in the maze throughout the study.

Some of the disturbances (difficulty in going through the maze with unlocked doors and increased number of refusals in development of the first skill) could be due to muscular weakness, which develops with hypokinesia [3]. We submitted this circumstance to comprehensive analysis in a study of the effects on rat VMA of space flight conditions aboard the Cosmos-690 biosatellite for an analogous period of time. We failed to demonstrate any correlation whatsoever between changes in maze indices and electric activity of extremal muscles. It may be assumed that, in this case too, the

In the experiment with an increased functional load, there were no reliable differences in indices of compared groups.

During development of the next two skills, virtually all of the animals worked without refusals, although the first group had a tendency toward deterioration of several indices, which was the most distinct in developing the third skill.

These data indicate that the first group of animals present reliable behavioral disturbances in the maze only for the first 6-7 days. The rest of the time they were statistically unreliable. However, the distinctly same direction of such changes in virtually all indices merits attention and special analysis.

The above disturbances were unrelated to a change in alimentary excitability of the

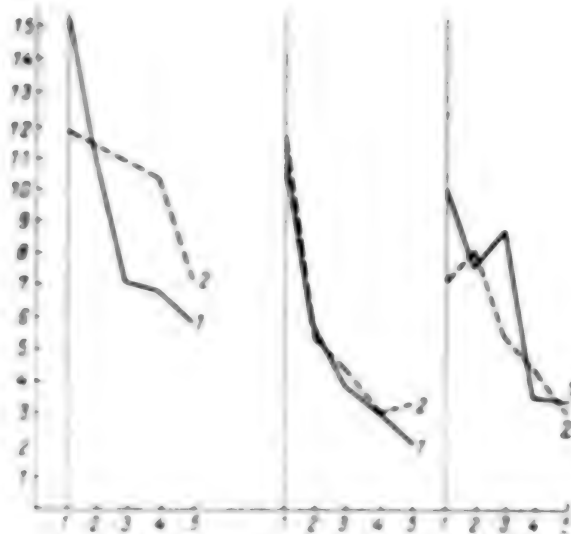


Figure 2.

Mean number of mistakes made by rats during development of first (a), second (b) and third (c) skills in going through maze with locked doors. X-axis, experiment No; y-axis, number of mistakes. Arrows point to 1st day of development of each skill.

from different receptors (first of all, muscular ones) may be excessive at the first stage of the readaptation period for the CNS that has been thus weakened, and this flow could induce protective, extraliminal inhibition, as a result of which the number of refusals would increase.

Our data disagree somewhat with the results obtained by L. N. Khruleva in a study of rat HNA [2]. She reports that there is severe and prolonged impairment of motor and alimentary conditioned reflexes after 30 days of restricted movement. The changes we found in HNA were significant and reliable only for 6-7 days, although they were observed for 22 days. This inconsistency may be due to the following causes: difference in duration of hypokinesia, differences in hygienic conditions when keeping the animals in the small boxes and, mainly, difference in sensitivity of methods used to evaluate HNA. It is known that, under the influence of the same factors, there is considerably more impairment of conditioned reflex activity than maze skills [7].

disturbances in the muscular system were not predominant in behavioral changes. This is also indicated by the fact that the first group of animals made reliably more wrong movements in the first run through the maze with locked doors than control rats, and this could hardly be possible if there were considerable muscular weakness.

The volume of muscular work was 5 times greater in the experiment with an increased functional load. Nevertheless, the first group of animals even behaved better in the maze than controls, which also indicates that the changes in the muscular system were unimportant to organization of the animals' behavior in the maze.

We believe that the changes we have described in the animals' behavior are attributable mainly to a change in functional state of the CNS related chiefly to sensory deprivation of the organism under hypokinetic conditions. The flow of information

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THE COMBINED EFFECT OF CARBON MONOXIDE AND HYPOKINESIA

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[English abstract from source]

In 1970, experiments were conducted with white rats exposed to a combined effect of carbon monoxide and hypokinesia. It was found that a concentration of 0.05-0.082 mg/l showed that the animals had significant hypokinesia-induced changes. It is concluded that the combined effect of carbon monoxide and hypokinesia is not additive.

[Text] Carbon monoxide and hypokinesia are permanent factors in small sealed habitats. It is imperative to investigate the distinctions of their successive and simultaneous effects on the organism in order to set the permissible levels of carbon monoxide in the artificial atmosphere of such objects.

It was previously discovered that preexposure to carbon monoxide has an aggravating effect on development of hypokinetic disorders in albino rats and, conversely, restriction of animal movement lowers their resistance to the acute effect of carbon monoxide [2].

However, until recently the combined effect on the body of carbon monoxide and hypokinesia had not been established.

In this report, we submit the results of an experimental study of this matter.

Methods

We conducted our study on 160 male albino rats with an initial weight of 160-170 g. The animals were divided into four groups. The first group consisted of rats exposed to carbon monoxide in a concentration of 0.05-0.082 mg/l, which was 2.5 times above the maximum permissible concentration (MPC) thereof in the air of work zones of industrial buildings

(20-24°C), continuously around the clock for 30 days; in the second group were animals who were kept for 1 month in hypokinetic cages; the third group of animals, in the same type of cage, were placed in the exposure chamber for 30 days and submitted to the same concentration of carbon monoxide; the fourth group spent 30 days in a chamber, through which we passed room air, without restriction of movements.

We examined experimental and control rats on the 10th, 20th and 30th days of the experiment. We recorded body weight and oxygen uptake according to N. I. Kalashnikov [3], erythrocyte count and hemoglobin level in peripheral blood, carboxyhemoglobin (in CO) content of blood by the method of Wolff [4]. Seven rats from each group were decapitated, and determination was made of succinate dehydrogenase (4,4'-D₂-succinate/acceptor/-oxidoreductase) and cytochrome oxidase (C₁-C₁'-cytochrome-C:O/-oxidoreductase) activity in hepatic tissue [5, 6].

Results and Discussion

As shown by the experiments, keeping growing rats around the clock in hypokinetic cages not only retarded weight gain, but lowered weight. Exposure to carbon monoxide of rats kept in hypokinetic cages for 30 days had an analogous effect on this parameter. With exposure of rats to carbon monoxide without restricting them in the chamber, they gained weight like the control group, and it is only on the 20th day of the experiment that their weight gain began to lag somewhat from that of intact rats (Figure 1a).

Oxygen uptake increased in rats kept in hypokinetic cages for 30 days, and this confirms previously obtained results [7, 8].

Continuous exposure to carbon monoxide elicited virtually no change in oxygen uptake by experimental animals. However, with exposure of hypokinetic rats to carbon monoxide they took up considerably more oxygen than animals kept in hypokinetic cages without exposure to carbon monoxide (Figure 1b).

Figure 2 illustrates the effect of these factors on respiratory enzymes of hepatic tissue in experimental rats.

The data in Figure 2 show that in rats exposed to carbon monoxide succinate dehydrogenase activity of hepatic tissue was above the base level, as well as above the level in control animals, on the 10th, 20th and particularly 30th experimental days. In the case of exposure to carbon monoxide of immobilized rats, succinate dehydrogenase activity of hepatic tissue was considerably lower on the 20th and 30th experimental days than in intact animals. Analogous changes in activity of this enzyme were noted in rats kept in hypokinetic cages for 1 month.

Cytochrome oxidase activity in hepatic tissue decreased under the influence of carbon monoxide (from a concentration of 0.0576-0.02 mg/l), which is consistent with data in the literature [7].

Table 1. Absorption spectra, fluorescence and absorbance-luminescence in rats exposed to the combination of carbon monoxide and hypoxia

Day	Hemoglobin, 100 cc		Hemoglobin, g/100		Carboxyhemoglobin, %			
	before expt.	after expt.	1-15	2-15	before expt.	1-15	2-15	1-15
2000	100.0	100.0	100.0	100.0	1.00 ± 0.1	1.20 ± 0.1	1.40 ± 0.2	1.51 ± 0.3
2000	100.0	100.0	100.0	100.0	1.00 ± 0.1	1.20 ± 0.1	1.40 ± 0.2	1.51 ± 0.3
2000	100.0	100.0	100.0	100.0	1.00 ± 0.1	1.20 ± 0.1	1.40 ± 0.2	1.51 ± 0.3

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Table 2. Degree of change in some hematological, biochemical and physiological parameters of animals under the combined effect of hypokinesia and carbon monoxide, 2

Case No.	Sex	Age	Date of admission	Hemoglobin	Erythrocytes	Activity of cytochrome oxidase, succ. dehydrogen.									
						1	2	3	4	5	6	7	8	9	10
Day of examination															
11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64
65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96
97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112
113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128
129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144
145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160
161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176
177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192
193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208
209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224
225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240
241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256
257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272
273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288
289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304
305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320
321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336
337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352
353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368
369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384
385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400
401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416
417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432
433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448
449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464
465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480
481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496
497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512
513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528
529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544
545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560
561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576
577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592
593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608
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625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640
641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656
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673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688
689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704
705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720
721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736
737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752
753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768
769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784
785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800
801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816
817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832
833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848
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865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880
881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896
897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912
913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928
929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944
945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960
961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976
977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992
993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1006	1007	1008
1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024
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1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104
1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120
1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134	1135	1136
1137	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152
1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168
1169	1170	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	1181	1182	1183	1184
1185	1186	1187	1188	1189	1190	1191	1192	1193	1194	1195	1196	1197	1198	1199	1200
1201	1202	1203	1204	1205	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216
1217	1218	1219	1220	1221	1222	1223	1224	1225	1226	1227	1228	1229	1230	1231	1232
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1249	1250	1251	1252	1253	1254	1255	1256	1257	1258	1259	1260	1261	1262	1263	1264
1265	1266	1267	1268	1269	1270	1271	1272	1273	1274	1275	1276	1277	1278	1279	1280
1281	1282	1283	1284	1285	1286	1287	1288	1289	1290	1291	1292	1293	1294	1295	1296
1297	1298	1299	1300	1301	1302	1303	1304	1305	1306	1307	1308	1309	1310	1311	1312
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1329	1330	1331	1332	1333	1334	1335	1336	1337	1338	1339	1340	1341	1342	1343	1344
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1361	1362	1363	1364	1365	1366	1367	1368	1369	1370	1371	1372	1373	1374	1375	1376
1377	1378	1379	1380	1381	1382	1383	1384	1385	1386	1387	1388	1389	1390	1391	1392
1393	1394	1395	1396	1397	1398	1399	1400	1401	1402	1403	1404	1405	1406	1407	1408
1409	1410	1411	1412	1413	1414	1415	1416	1417	1418	1419	1420	1421	1422	1423	1424
1425	1426	1427													

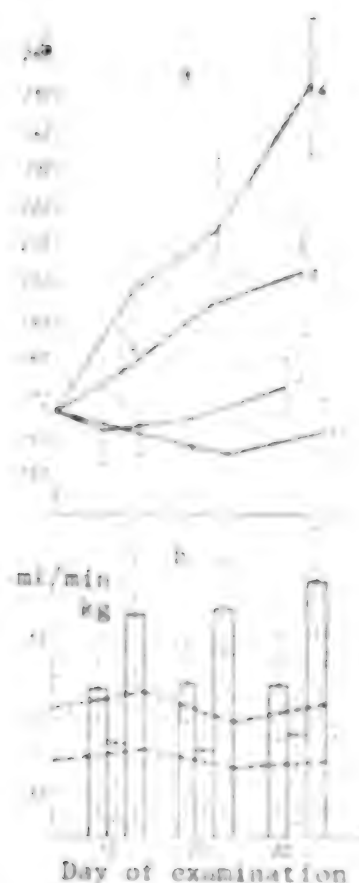


Figure 1.

Effect of separate and combined carbon monoxide and hypokinesia on dynamics of albino rat body weight (a) and intensity of oxygen uptake (b). Here and in Figure 2:

- 1) hypokinesia
- 2) carbon monoxide
- 3) hypodynamia and carbon monoxide combined
- 4) control

the factors studied in the demonstrated effects of a combination thereof (Table 2).

As can be seen in Table 2, there are different shares of involvement of organized (A+B+Ab) and random factors in formation of the parameters under study. For this reason, when making a quantitative evaluation of the results of our study we took into consideration only the parameters upon which organized experimental factors had a considerably greater influence

However, carbon monoxide had a different effect on this parameter in rats put into the hypokinetic cages: on the 10th day, cytochrome oxidase activity of hepatic tissue of experimental animals was virtually the same as the base level; on the 20th day, enzyme activity exceeded significantly both this level and the level of this parameter in intact rats; however, by the end of the experiment, cytochrome oxidase activity was comparable to the initial level. Analogous changes in activity of this enzyme were demonstrable in hypokinetic animals that were not exposed to carbon monoxide.

Table 1 lists the hematological parameters of experimental rats in all four groups. Some tendency toward erythrocytosis and hyperhemoglobinemia was noted in animals exposed to carbon monoxide alone. With the combination of carbon monoxide and hypokinesia, as well as the latter alone, hemoglobin and erythrocyte count were virtually the same as in intact rats. Blood carboxyhemoglobin level was virtually the same in all groups.

The foregoing warrants the conclusion that, in the case of a combination of 30-day hypokinesia and carbon dioxide in a concentration of 0.05 ± 0.002 mg/l, the latter has no appreciable effect on the set of changes that develop in rats when their movements are restricted for a long period of time. This conclusion is confirmed by the results of variance analysis [10, 11], which characterizes quantitatively the share of involvement of each of

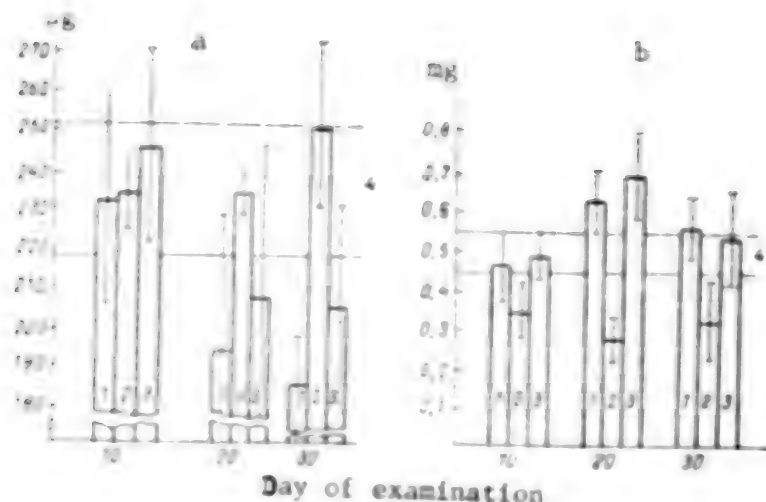


Figure 2. Activity of succinate dehydrogenase (a) and cytochrome oxidase (b) in hepatic tissue of albino rats under the separate and combined effects of carbon monoxide and hypokinesia

than random factors. The results of such an evaluation revealed that, in the case of the combined effect of carbon monoxide (factor A) and restricted motor activity (factor B), body weight of growing rats and intensity of oxygen uptake at all observation times were determined by the influence of the latter factor, whereas hemoglobin level of blood was, on the contrary, determined by factor A. Each of the organized factors acquired or lost its dominant significance at specific times, with regard to overall effect on activity of cytochrome oxidase of hepatic tissue. Thus, factor A, carbon monoxide had a stronger influence on activity of this enzyme on the 10th experimental day (18.2% versus 7.3% for factor B); on the 20th day, however, involvement of factor B in the demonstrated effect increased by 60.9%, while the effect of factor A diminished to 5.2%. Such a correlation between the effects of factors A and B on cytochrome oxidase activity of hepatic tissue persisted (though it was less marked) on the 30th experimental day as well.

The obtained data from quantitative analysis of overall effects of the combination of factors indicate that hypokinesia is of predominant significance to formation of most of these effects. Against the background of hypokinesia, there is no manifestation of the effect of carbon monoxide in a relatively low but biologically significant concentration, 0.05-0.002 mg/l. This could be attributable, to some extent, to its insignificant influence on the set of compensatory and adaptive mechanisms that allow the organism to adapt to a new level of function of its physiological systems in the case of prolonged restriction of movements.

Thus, in the case of a 30-day combination of hypokinesia and carbon monoxide, the MPC of the latter does not require revision.

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LEVELS AND PROPORTION OF RNA AND PROTEINS IN THE SYSTEM OF THE NEURON--
VESTIBULAR NUCLEAR NEUROGLIA AND CEREBELLUM DURING HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5,
1979 pp 49-53

[Article by L. M. Mamalyga, submitted 22 Mar 77]

[English abstract from source]

It has been demonstrated cytochemically that even a short term hypokinesia affects significantly the content of RNA, total and individual proteins in the cell structures of the vestibular nuclei (Beydterev and Deiters nuclei) and of the cerebellar cortex. The changes in these substances depend on both the type of the stress effect and the morphofunctional organization of the brain structure.

[Text] In the numerous works dealing with the effect of hypokinesia on the body, not infrequently we encounter information to the effect that prolonged restriction of movements has a substantial effect on the function of the vestibular analyzer [1-5]. The early stage of hypokinesia, which proceeds against the background of a marked stress reaction associated with stressed CNS [central nervous system] function (as well as that of most other systems of the body), differs substantially from the subsequent period of adaptation [6-8]. There have been virtually no studies as yet of the state of the central element of the vestibular analyzer at the early stage of hypokinesia.

Neurochemical parameters, in particular RNA and protein content, are being used more and more to assess the direction and severity of changes in functional activity of cellular elements of the brain [9-12].

Our objective here was to investigate the levels and proportion of RNA, total and basic proteins in neurons and glial cells (Bekhterev and Deiters nuclei), as well as the cerebellar cortex, which is closely related to them, in the presence of varying degrees of brief restriction of motor activity.

Methods

Experiments were conducted on standard male Wistar albino rats weighing 160-180 g (5-6 months of age). In order to create hypokinetic conditions, the

rats were put in wire cages conforming to the size of the animals, and this restricted their movements severely. Total immobilization was obtained by securing the head, legs, trunk and tail to special devices. The animals were in prone position. They were kept in a hypokinetic state and immobilized for 14 hr. By this time, maximum increase in free blood catecholamine fractions is observed [13]. We used six animals in each series of experiments.

After termination of the experiments, the rats were decapitated without use of anesthesia, the medulla and cerebellar hemispheres were extracted under refrigeration, then fixed in cooled Bindschly fixing agent (formalin, ethanol and water acid in a ratio of 9:3:1). After the usual histological treatment of tissue and imbedding it in paraffin, we prepared serial sections 5-10 μ m thick. Some of the sections were stained for RNA with gallocyanine and ammonium cerotic sulfate according to Einerson in the modification of Gerube et al. [14] and the rest was stained for total and basic proteins with toluidine black 10b, which bound stoichiometrically with one or the other, depending on the pH of the staining solution [15-17]. The concentration of RNA and proteins was determined by the optical density of cytoplasm of neurons and body (virtually the nuclei) of neuroglial satellite cells at a distance of no more than 3-4 μ m from the body of the neuron. Determination of concentration of RNA and proteins (in arbitrary units) was made in the visible part of the spectrum using a probe cytospectrophotometer designed by L. N. Agreikin et al. [18], with some modifications [19] (probe 4 μ m in diameter, wavelength 525 nm for RNA and 620 nm for proteins). Light transmission of dye stoichiometrically bound with RNA or proteins was determined at four diametrically opposite points in each neuron. We examined 45 neurons and 45 gliocytes from different parts of the brain of each animal, and this is quite sufficient for cytochemical analysis [12].

We determined the amount of tested substances (as percentage of control taken as 100%) scaled to the cytoplasm of one neuron (or glial cell) as the product of the relative volumes multiplied by optical density. We sketched in the cell population (neural and glial) of each part of the brain using an MRS-1 microprojector device (objective 50 \times , ocular 10 \times). Calibration was performed by means of a millimeter object in such a manner that 1 μ m on the preparation corresponded to 1 μ m on the screen. This enabled us to measure the large and small diameters of neurons, their nuclei and glial cells (the volume may be expressed in cubic micrometers). The volume of neuronal cytoplasm was expressed as the difference between volume of the cell and its nucleus calculated by the formulas for a triaxial ellipsoid [20] and ellipsoid of revolution, respectively. The volume of gliocytes was calculated by the formula of ellipsoid of revolution [21].

We examined the cellular distribution of Betkyrev and Deiters nuclei, as well as Purkinje cells, the cerebellar cortex and their gliocytes. The distribution of the nuclei were determined from a lightmicrograph atlas [21, 22]. Large and medium-sized neurons were examined in the same proportion as gliocytes.

All of the digital material was submitted to statistical processing according to Student-Fisher.

Results and Discussion

Functional loads on the nervous system lead to a change in metabolism of its cellular structures, which is associated with changes in their volume that are related to differences in hydration and dehydration of cells, as well as intensity of process of synthesis and dissociation [12, 23-26]. For this reason, to solve the problem set forth, the results of morphometric readings could provide some information, along with cytophotometric data.

No statistically reliable changes were demonstrated during hypokinesia in neurons and glial cells of Bekhterev's nucleus. In the neurons of Deiters' nucleus an increase in nucleus volume (by 20%) and significant decrease in RNA, total and basic protein content of neuronal cytoplasm, as well as total and basic proteins in gliocytes were demonstrated (Table 1, Figure 1).

Table 1. Volume of cytoplasm and nuclei of neurons (μm^3) in different parts of the brain of intact and experimental animals

Brain structure examined	Control	Hypokinesia		Immobilization	
		Mean	P	Mean	P
Bekhterev's nucleus	1708 ± 112 480 ± 31	1309 ± 77 374 ± 26	>0.1 >0.2	12047 ± 514 382 ± 21	<0.05 <0.02
Deiters' nucleus	1158 ± 37 1812 ± 36	1864 ± 46 1289 ± 42	>0.2 <0.05	10635 ± 85 1237 ± 72	>0.05 >0.2
Granular (pyramidal) cells	256 ± 46 187 ± 37	325 ± 74 305 ± 13	>0.2 <0.01	256 ± 72 462 ± 13	>0.1 <0.01

Note: Cytoplasm volume in numerator and nucleus volume in denominator.

As can be seen in Tables 1 and 2, immobilization led to an increase in volume of cytoplasm and nucleus of neurons (by 22 and 20%, respectively) and some decrease in volume of gliocytes in Bekhterev's nucleus. There was a decrease in total protein of neuronal cytoplasm and a tendency toward decrease in RNA and basic proteins. The changes were somewhat different under the same conditions in the vestibular nucleus of Deiters. Here, morphometric readings failed to demonstrate reliable changes in volume of neuronal nucleus and cytoplasm, while cytochemical data were indicative of marked decrease in RNA, total and basic protein content, both in neuronal cytoplasm and glial cells, the volume of which was diminished too (Figure 1, Table 2).

With both hypokinesia and immobilization, there was a decrease in volume of glial cells, as well as nuclei of Purkinje cells in the cerebellar cortex,

with unchanged volume of their cytoplasm (see Tables 1 and 2). Immobilization induced a decrease in RNA and basic protein content, both in neuronal cytoplasm and gliocytes, while hypokinesia did so only in glial satellite cells (Figure 2).



Figure 2. Changes in RNA (1), as well as total (2) and basic (3) protein content in different cellular structures of the brain in the case of hypokinesia (I) and immobilization (II).

a) Bekhterev nucleus

b) Deiters' nucleus

Here and in Figure 2: white columns, neurons; striped columns, glia. Y-axis, changes in levels of substances studied (% of control taken as 100%). Vertical lines, doubled standard error (2σ).

Table 1. Volume of gliocytes (μm^2) in different parts of the brain of intact and experimental animals

Brain structure examined	Control	Hypokinesia		Immobilization	
		<i>n</i>	<i>P</i>	<i>n</i>	<i>P</i>
Bekhterev nucleus	870 ± 18	872 ± 13	>0.7	882 ± 15	<0.05
Deiters' nucleus	1012 ± 14	982 ± 8	>0.1	781 ± 12	<0.01
Cerebellar cortex	1457 ± 17	1179 ± 12	<0.005	1087 ± 9	<0.05

Thus, different degrees of inactivity (immobilization and hypokinesia) had different effects on RNA and protein content of cellular structures of the brain regions examined.

At the same time, there were also differences in metabolic responses of Bekhterev and Deiters nuclei to the same factor. Evidently, the demonstrated cytochemical differences between these nuclei could be closely related to the previously described [12] morphofunctional differences.

Current conceptions of functional and metabolic correlations in the neuron-glia system indicate that, at the stage of intensified neuronal function, there may be migration into the neuron of some substances from surrounding glial

satellite cells. It is maintained by a number of authors [9, 11, 12, 23, 27] that such a mechanism provides for a high level of functional activity of the neuron, in the presence of some states of the central nervous system, when the neuron's synthetic system is no longer capable of independently satisfying its requirements with regard to certain substances. It can therefore be assumed that the decrease in RNA and basic protein content of gliocytes of the cerebellar cortex in the presence of hypokinesia could be related to migration of a part thereof into neurons, which compensates to some extent the loss induced by a change in functional state of neurons. Immobilization of the animals led to a decrease in RNA content, not only in the neuroglia but in the cytoplasm of Purkinje cells. Hypokinesia did not lead to changes in RNA and protein content in the neuron--Bekhterev nuclear glia system, whereas immobilization induced a drastic decrease in levels of the tested substances in gliocytes of this nucleus. The persistent decrease in RNA and protein content, not only in neurons but in surrounding glial satellite cells, is indicative of depletion of the protein biosynthesizing apparatus of the neuron-glia system.



Figure 2.
Change in RNA (1), total (2) and basic protein (3) content of cellular structures of the cerebellar cortex during immobilization (a) and hypokinesia (b)

The decrease in RNA and protein content demonstrated in most cases in some cells is apparently related more to changes in the hormonal background, which occur under the influence of stress factors, than to the specific influence of immobilization or hypokinesia. The change in functional state of the adrenal cortex and hypophysis, which was demonstrated with brief restriction of motor activity and which leads to a drastic increase in ACTH and corticosteroid content of blood and nerve tissue [11, 28], could lead to intensified breakdown of the substances studied in cellular structures of the brain. Such a mechanism is possible in the vicinity of centers of neural secretions [29-31].

Most often, the changes in RNA and protein content were in the same direction (100% increase, 100% decrease) and not necessarily demonstrated between them.

Thus, the obtained data indicate that even brief restriction of motor activity has a substantial effect on RNA and protein content of the neuron-glia system. The nature of the changes in these compounds was related both to the type of the gliocyte (neuron or neuroglia) and to the type of the cell. As for RNA of the neuron-glia system, it is known.

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SOME HEMODYNAMIC PARAMETERS DURING RESPIRATION OF OXYGEN UNDER EXCESSIVE PRESSURE

MOSTOW KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 53-57

[Article by K. I. Murakhovskiy and L. I. Letkova, submitted 4 Mar 77]

[English abstract from source]

The authors give the experimental design, the pattern and value of respiration during the use of oxygen at pressures of 10 and 15 atmospheres (10 and 15 MPa) in subjects breathing at specified pressures of 25 mm Hg. The data on hemodynamic parameters were registered by the method of radiopaque contrast angiography. During the study the test subjects showed an average 27% decrease in the volume of blood flow in the coronary arteries. The test subjects who were subjected to the specified pressure showed a decrease in the volume of blood flow in the coronary arteries. It is suggested that the decrease in the volume of blood flow in the coronary arteries was mainly induced by the increase in the pressure in the coronary arteries. It is concluded that the reduction in the volume of blood flow in the coronary arteries is the result of the increase in the pressure in the coronary arteries.

[Text] The wide use in aviation practice of hyperbaric oxygen is the reason for the interest of researchers in this problem [1-4]. As we know, the main objective of breathing high pressure oxygen is to assure the required level of oxygenation of the pilot's body in the case of depressurization of the cabin of an aircraft at altitudes above 12,000 m. However, there are several physiological limitations on the use of hyperbaric breathing. Among them, hemodynamic disturbances were in one of the leading places, and very often they are the ones that limit endurance of specified modes of excess pressure. The importance of continuing research in this direction is unquestionable.

Methods

In this work, we used the radiopaque method to study the reactions of the human cardiovascular system to breathing oxygen at uncompensated excess pressure (10 and 15 MPa (10 and 15 mm Hg)). This method makes it possible to obtain adequate information about the quantitative changes in the main parameters of the circulatory system.

The radiocardiogram (RKG) was recorded on a type NS-110 radiocirculograph. The collimated scintillation sensor of the instrument was centered in the region of the heart at the level of the fourth intercostal space along the parasternal line. An ^{51}Cr -labeled albumin solution was used as an indicator. Activity of the single dose used for examination constituted 25-30 μCi . In order to determine the area under the RKG curve required for subsequent calculation of hemodynamic parameters, we used the analytical processing method with a digital computer by the somewhat modified method proposed by F. F. Kapeiko et al. [5].

Minute volume of the heart (MV) was calculated with the formula of N. Veall et al. [6]. In addition, we determined the minute or cardiac index (CI), stroke volume of the heart (SV), stroke index (SI), pulmonary lung volume (PLV) using the formula proposed by Z. Donato et al. [7], venous flow time in the ulnar vein--right heart segment, arterial flow time in the left heart--femoral artery segment, total peripheral resistance (TPR) and cardiac function (A).^{*} In the course of the study we recorded arterial pressure (AP), heart rate (HR) and respiratory rate (RR). Using the method of dilution of radioactive indicator, we used the conventional formulas in all tests to calculate circulating blood volume (CBV) and circulating plasma volume (CPV). All of the digital material was subjected to statistical analysis by the method of comparison of sets with pair-related variates for a probability of 0.95.

This study was performed on 20 healthy males ranging in age from 25 to 30 years. Each of them was submitted to a background examination, during which the basic hemodynamic parameters were obtained. The actual study was carried 2-3 weeks after the background examination, when we recorded the hemodynamic parameters while the subjects breathed oxygen under uncompensated pressure of 4.0 kPa for 10 min. All of the test and background studies were conducted with the subjects sitting down. In the test studies, the radiopaque tracer was administered 1.5-2 min after slow (30-40 s) attainment of the specified mode of excess pressure.

RESULTS AND DISCUSSION

Table 1 shows the results of our work. Respiration of oxygen at uncompensated excess pressure in the tested mode induced a significant and statistically reliable decline of MV by a mean of 15% ml ($P < 0.01$).^{**} There was a corresponding decline of CI, a parameter that characterizes MV referred to the unit of body surface. In all of the tests with excess pressure,

^{*} We used modified software, but with correction for level of excess (mm) pressure, CI (ml/min/m²) and SI.

^{**} We used a modified, two-sided Wilcoxon nonparametric test for the paired data.

there was a reliable decline of SV and SI by a mean of 31.6 ml and 16.3 ml/m^2 , respectively, i.e., b, almost 40% of the base value.

Table 1. Some parameters of blood flow rate

Index	Blood flow time in ulnar vein--heart segment, s		Blood flow time in pulmonary circulation, s		Blood flow time in heart--femoral segment, s	
	back-ground	excess pressure	back-ground	excess pressure	back-ground	excess pressure
M	24	6.9	4.7	4.0	9.5	7.8
SD	3.5	4.2	1.0	1.3	3.5	2.2
CI	4.4	3.2	0.9	1.2	3.2	2.0
AM		4.5		0.7		1.7
SD _{AM}		1.4		0.3		0.6

Key for this and Table 2:

M) arithmetic mean

SD) standard deviation

CI) confidence interval for $P = 0.95$

(M) mean deviation

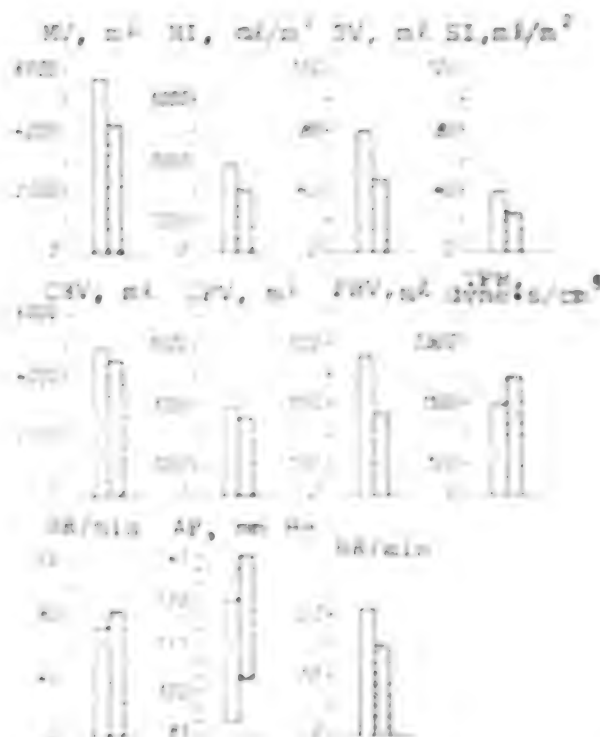
SD(M) standard error of mean deviation

Table 2. Parameters of cardiac function

Index	A_1 , kg-m/min		A_2 , kg-m/systole		A_3 , kg-m/ml	
	back-ground	excess pressure	back-ground	excess pressure	back-ground	excess pressure
M	8.7	1.5	0.41	0.07	0.00138	0.00141
AM		1.1		0.01		0.00011
SD _{AM}		0.2		0.005		0.00001

In addition, while breathing under excess pressure we observed a statistically reliable decline of CBV and CPV, rate of blood flow in the venous systemic circulation and RR. As compared to base values, there was also an increase in HR, AP, and flow rate in the pulmonary circulation and arterial compartment of systemic circulation, with significant increase in TPR (see Figure and Table 1).

As we know, breathing under excess pressure, which elevates intrapulmonary pressure, leads to elevation of pressure in vessels of the pulmonary circulatory system and chambers of the heart. As a result, there is ejection of a certain amount of blood from the pulmonary circulation into the vessels of systemic circulation [8, 9], as indicated also by the statistically reliable decline of CBV recorded in our studies (see Figure).



Changes in main hemodynamic parameters in man while breathing oxygen at uncompensated excess pressure. White columns, background; striped, hyperbaric oxygen.

only. The rather wide individual scatter of changes in MV, SV and other parameters demonstrated in our tests is most likely attributable to the fact that the subjects we used differed in degree of conditioning for breathing under excess pressure. Accordingly, the most marked hemodynamic changes were observed among those who participated for the first time in such tests. The changes were considerably less marked in well-conditioned subjects.

As we know, if all conditions being equal, MV is determined by the magnitude of output forced to the heart. The latter, as it has been demonstrated [11], is proportional to the difference between mean systemic pressure in the vascular system and pressure in the right atrium, and inversely proportional to the resistance to venous inflow. In turn, the vascular resistance between mean systemic pressure and pressure in the right atrium is determined by COV and therefore is proportional to the capacity of the vascular system. The driving of a pump by a pressure difference

Guyton [10] believes that breathing at excess pressure of 15-25 mm Hg, with rather slow elevation of pressure in the lungs, leads to elevation of mean systemic pressure to 25-30 mm Hg. In his opinion, this is attributable to the following factors: strong muscular contraction to implement expiration; shifting of blood from vessels in the pulmonary circulation to the left heart and vessels in the systemic circulatory system; excitation of the sympathetic nervous system (increase in peripheral vascular tension, increased force and rate of cardiac contractions, etc.).

In the opinion of Carr and Essex [11], compensatory mechanisms provide for retention of MV on virtually the base level for a rather long period of time in the presence of excess pressure at 15-25 mm Hg.

The results of the studies also revealed that by far not every organism copes with perturbances in the circulatory system at such levels of excess pressure. In most subjects, the compensatory mechanisms performed their task to a greater or lesser degree

In our studies, we demonstrated decrease of CBV by a mean of 400 ± 134 ml, or approximately 37%, as compared to the base level. At the same time, it is known that a decline of CBV by the same 8-9% in animals (dogs) under total spinal anesthesia and with continuous infusion of epinephrine to maintain normal vascular tone causes a decrease of MV to almost one-half the base level [22]. Thus, only a decrease in CBV can lead to decrease in "venous inflow" and, ultimately, MV. In our studies, the decline of MV was also aggravated by the increase in capacity of peripheral vessels as a result of elevation of mean systemic pressure, as a consequence of which part of the blood was deposited in the most "submissive" peripheral regions, leading to development of venous stasis. In this regard, the demonstrated increase by a mean of 371 ± 27 dynes/cm², or by 1.2 times, in total peripheral pressure, as compared to the base level of this parameter, is also significant.

The obtained data confirmed the existing opinion that the functional state of the heart proper and its autonomic regulatory mechanisms are on a rather high level under the tested mode of excess pressure, and they are not the prime cause of decrease in MV. This was indicated, in particular, by the direction of changes in AP, pulse pressure, HR and rate of arterial blood flow (see Figure and Table 1). Of interest in this regard is also the nature of changes in so-called specific cardiac function, an estimated parameter characterizing the work (in kg-m) performed by the heart with ejection of 1 ml blood (see Table 2, A₃). The obtained data indicate that, in spite of decline of parameters of heart work performed per ejection, the "specific" work of the heart when breathing under excess pressure shows virtually no change. The latter would hardly be possible if there were development of functional insufficiency of the heart.

Thus, the decrease in MV is determined primarily by elevation of pressure in the chambers of the heart as a result of the factor used. In turn, elevation of pressure in the pulmonary circulatory system and in the heart leads secondarily to elevation of mean systemic pressure and development of signs of deposition of blood, as a result of which there is a decrease in CBV. The latter circumstance maintains MV at a lower level than initially, even with established equilibrium in the system.

The obtained material is consistent with data in the literature, and it indicates that, even with a relatively low level of excess pressure, the regulatory mechanisms do not fully compensate for the changes that occur in the circulatory system under such conditions.

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BICHROMATE OXIDABILITY AS A CRITERION OF QUANTITATIVE LEVELS OF ORGANIC IMPURITIES IN RECLAIMED WATER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 57-61

[Article by V. A. Kryuchkov and N. S. Mareyeva, submitted 31 Mar 77]

[English abstract from source]

The article describes the method of determining the bichromate oxidability of drinking water, which is a criterion of quantitative levels of organic impurities in it. The method is based on the use of potassium dichromate as an oxidizing agent. The results of the experiments show that the bichromate oxidability of drinking water is a reliable criterion of the degree of pollution by organic impurities. The method is simple and does not require special equipment. The results of the experiments show that the bichromate oxidability of drinking water is a reliable criterion of the degree of pollution by organic impurities. The method is simple and does not require special equipment.

[Text] Oxidability of drinking water, which is a criterion of quantitative levels of organic impurities in it, is one of the important indices of water quality. In the practice of testing water for pollution by organic impurities, the main methods used involve determination of permanganate and bichromate oxidability. It is known that permanganate oxidizes only a small part of organic impurities in water, whereas potassium bichromate oxidizes most contaminants of water. Several authors have made a quantitative assay of degree of oxidation of different organic substances that pollute potable, natural water and liquid sewage. Work is continuing in this direction, and methods are being refined for performing analyses [1-3].

Our objective here was to make a quantitative assay of degree of oxidation of impurities that may pollute water reclaimed from the products of vital functions of man.

Methods

In the experiments, we used solutions of different chemical compounds prepared from chemically pure reagents in distilled water. We used preparations

of polyvinylformal mechanically dispersed in distilled water and an aqueous extract of polyvinylformal. The concentrations of products of polymer breakdown were determined, in this case, by the weighing method after evaporation of water. We also used reclaimed water obtained by the method of sorptive purification of a condensate of atmospheric moisture.

The following methods were used to determine oxidability of the solutions:

1) Method of determination of permanganate oxidability of water in an acid medium according to GOST 4593-49.

2) Method of determination of bichromate oxidability of water involving 2-h boiling of the sample with a reflux condenser. In this method, water impurities are submitted to bichromate oxidation by addition to the reaction mixture 50 vol.% concentrated sulfuric acid in the presence of a catalyst, silver sulfate (0.3-0.4 g/20 ml sample). Addition to the reaction mixture of 0.4% bivalent mercury sulfate enables us to avoid oxidation of chlorides. In several countries, this method is used as the standard for determining oxidability of potable, natural water and liquid sewage [2].

3) Nonstandard method, which differs from the second one in that the samples are heated over a boiling water bath without adding the catalyst to the sample.

The results of test readings were submitted to processing. We calculated the arithmetic mean value of oxidability and standard deviation.

Results and Discussion

The results of the tests, which are listed in Table 1, indicate that potassium permanganate does not oxidize main impurities of water when the reaction is run under standard conditions. There is only 10-15% oxidation of several other impurities, in relation to maximum oxidation thereof in cathodic acid (without chlorine) and water.

For this reason, low degree of permanganate oxidability of reclaimed water that has sorptive purification involves to some different degree depends mainly on the composition of impurities and presence of readily oxidizable substances in them. Accordingly, permanganate oxidability can only be used as a qualitative indicator of pollution of reclaimed water by oxidizable impurities.

Unlike permanganate, potassium bichromate (K₂Cr₂O₇) of the tested organic impurities, with few exceptions, without exception. Most of the impurities are 70-100% oxidized by potassium bichromate. There is practically complete oxidation of water specifically treated by reclaimed water as method described, products of decomposition and mechanical breakdown of polyvinylformal, and formaldehyde. According to results of tests, low oxidability of oxidability of organic impurities.

Table 1. Oxidability of solutions (100 mg/l) of some possible impurities in reclaimed water (M₂O; in mg O₂ per liter)

water impurity tested	Estimated oxygen minimum with oxidation to CO ₂	Method of determining oxidability	
		permanganate	2-h boiling with bichromate
Methyl alcohol	150.0	2.8±0.7	148.8±2.4
Ethyl alcohol	208.7	11.0±2.2	198.8±1.6
Formaldehyde	106.6	105.0±8.7	106.4±1.3
Acetaldehyde	181.8	40.4±1.4	176.9±5.5
Acetone	220.6	1.5±0.1	218.6±2.9
Acetic acid	168.6	0.0±0.0	103.7±2.3
Propionic acid	151.0	1.8±0.0	147.3±6.1
n-Butyric acid	181.8	11.6±0.6	174.0±1.8
Ethyl ether	259.4	5.2±0.2	182.6±1.1
Ethyl acetate	181.8	21.6±1.1	148.6±5.3
Phenol	238.2	219.8±4.3	227.7±5.1
Benzene	307.6	0.7±0.2	50.4±1.8
Polyvinylformal	190.0	—	189.0±10.1
	(8% acetylation)		
Water extract of polyvinyl-formal	Unstable	33—36	122—152
Urea	—	0.6±0.2	51.6±5.5
Ammonia	—	0.8	0±0.3

In the last few years, the method of determination of bichromate oxidability was refined to some extent. The improvement consisted of the fact that, for effective prevention of oxidation of metal chlorides, bivalent mercury sulfate was added to the reaction mixture (0.4 g per 20 ml sample). Bivalent mercury forms a molecular compound with chloride ions that is not oxidized by potassium bichromate. There is negligible probability of pollution of reclaimed water by chlorides; however, they could be intentionally added to purified water to enrich it with mineral salts. We evaluated the effect of mercury sulfate on oxidation of chloride ions and on the results of determining oxidizability of reclaimed water with low mineral content. Table 2 lists the results of tests on oxidation of metal chlorides contained in solutions and reclaimed water. The data given in Table 2 indicate that silver sulfate, when added to the reaction medium as a catalyst for oxidation of organic impurities, is also an agent that prevents oxidation of chloride ions. When the chloride concentration is up to 25 mg/l, one can disregard the influence thereof on the results of determining the oxidability of reclaimed water. It is desirable to use mercury sulfate with higher concentrations of chlorides.

We determined oxidability of organic substances by the above method, which differed in that the test sample was heated with bichromate over a boiling water bath.

Table 2. Bichromate oxidability of chloride solutions (mg O₂/l)

Chloride solutions	Modification of method		
	without Ag ₂ SO ₄	with Ag ₂ SO ₄	with Ag ₂ SO ₄ + H ₂ SO ₄
With 0.25 N reagent K ₂ Cr ₂ O ₇			
KCl with Cl ⁻ concentration of 100 mg/l	24.8 σ = ±1.4	1.9 σ = ±0.1	0
KCl with Cl ⁻ concentration of 25 mg/l	14.3 σ = 0	0 (below sensitivity of method)	0
With 0.025 N reagent K ₂ Cr ₂ O ₇			
KCl with Cl ⁻ concentration of 25 mg/l	6.0	1.2	0
Reclaimed water containing 25 mg/l chlorides	—	46.6	46.0

Table 3. Oxidability of solutions (100 mg/l) of some possible impurities in reclaimed water determined by the method of heating samples with bichromate at a temperature of 100°C (M-σ, mg O₂/l)

Tested impurity of water	Oxidability
Methyl alcohol	18.0 ± 2.4
Ethyl alcohol	18.5 ± 1.7
Formaldehyde	18.1 ± 1.7
Acetaldehyde	18.1 ± 1.9
Acetone	18.2 ± 1.2
Acetic acid	17.7 ± 1.4
Propionic acid	17.8 ± 2.1
n-Butyric acid	18.0 ± 1.6
Ethyl ether	18.4 ± 2.4
Ethyl acetate	17.7 ± 1.8
Thiophene	17.7 ± 1.8
Hexane	17.7 ± 1.9
Phenylaldehyde	18.0 ± 1.8
Grease	18.0 ± 1.1

According to Table 3, most impurities in reclaimed water are oxidized to a much lesser extent in this case. It was also established that using silver sulfate as a catalyst at a temperature of 100°C does not have an appreciable effect on oxidation of organic substrates. Consequently, oxidation of organic impurities in water by potassium bichromate to carbon dioxide is achieved under three conditions: not high acidity of oxidizing

medium (30 vol.% H_2SO_4); high temperature of reaction mixture, which reaches 150-170°C during boiling with 50 vol.% H_2SO_4 with reflux condenser; use under these conditions of a catalyst for oxidation of organic impurities in water (Ag_2SO_4).

The correlation between extent of bichromate oxidability of water and concentration (mass) of organic impurities that pollute water varies. It is specific for each chemical compound. Table 4 shows that 1 mg absorbed oxygen could correspond to the following mass of impurities: 0.46 mg acetone, 0.94 mg formaldehyde, 1.94 mg urea, etc. The mean conversion coefficient depends on the quantitative and qualitative composition of impurities.

Table 4. Correlation between degree of bichromate oxidability (experimental figures from data in Table 1) and concentration (mass [weight]) of organic impurities in water

Organic compound	Ratio of concentration of impurity (mg/l) to oxidability of solution (mg O_2 /l)
Methyl alcohol	0.67
Ethyl alcohol	0.50
Formaldehyde	0.94
Acetaldehyde	0.57
Acetone	0.46
Acetic acid	0.92
Propionic acid	0.68
n-Butyric acid	0.58
Ethyl ether	0.55
Ethyl acetate	0.67
Polyvinylformal	0.53
Products of polyvinylformal breakdown	0.76-0.82
Arithmetic mean of 12 indices	0.656

For water reclaimed from a condensate of atmospheric moisture, the ratio of mass or concentration of impurities to bichromate oxidability is about 0.66. This ratio is calculated as the arithmetic mean for 12 potentially possible impurities in reclaimed water (see Table 4).

Since reclaimed water, initial and intermediate products serving to reclaim water have a variable composition, quantitative determination of the sum of organic impurities by the method of bichromate oxidability can be made only in study water with a known set of oxidable ingredients.

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AMOUNT OF MICROORGANISMS DISCHARGED FROM THE UPPER RESPIRATORY TRACT AND
INTEGUMENT OF PEOPLE CONFINED IN A SEALED CHAMBER

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1979 pp 61-65

[Article by S. N. Zaloguyev, A. N. Viktorov, K. V. Zarubina and V. P.
Gorshakov, submitted 24 Jun 77]

[English abstract from source]

The authors have studied microorganisms discharged into the ambient environment from the upper respiratory tract and integument of people confined in a sealed chamber. They found a correlation between the rate, on the one hand, and the microclimate parameters and hygienic measures used, on the other. The data obtained during the study will be used in the design of air purification systems.

[Text] During space flights, along with autoinfectious diseases, there may be exogenous or "cross" infections due to exchange of microorganisms between individuals [1-8].

The spread of the infectious agent depends largely on the characteristics of the first stage of the mechanism of transmission of infection, namely intensity of migration of the pathogen into the environment.

This circumstance makes it necessary to conduct research directed toward quantitative determination of processes of elimination of microorganisms from the upper respiratory tract and skin of individuals when they are in a sealed room, as well as the influence on this process of some factors inherent in space flights.

Methods

We conducted two 10-day studies in a 24 m³ sealed chamber with the participation of 8 subjects. The program for study No 1 provided for alteration of microclimate parameters in the chamber: elevation of temperature to 35°C and relative humidity to 90% for 14 days. At the first stage of study No 2, use of personal hygiene measures was completely restricted for 10 days; at the second stage, air temperature in the chamber was held at 18±1°C for 10 days; relative humidity constituted 75-80%.

At the rest of the stages of the studies, optimum microclimate parameters were set in the chamber: air temperature $20 \pm 2^\circ\text{C}$, humidity 30-70%.

Just prior to the studies, the sealed chamber was submitted to mechanical cleaning, surfaces were cleaned with 1-1.5% aqueous solution of hydrogen peroxide and the air was exposed to ultraviolet light from a BLV-30 lamp for 1.5 h.

Determination of amount of microorganisms discharged from the subjects' upper respiratory tract and integument was made 9 times during the studies, as well as in the background period and 1-3 days after the subjects got out of the sealed chamber.

Quantitative evaluation of intensity of discharge of microorganisms was made in the following manner: open Petri dishes with nutrient medium (5% blood agar) were placed right in front of the upper respiratory tract of the subjects. The assays were made with the subjects breathing calmly for 5 min, then performing exercises for 5 min and reading a standard text (articulation) for 2 min.

In order to determine the amount of microorganisms discharged from the integument, 3 cm² disks were attached to the skin with adhesive tape; the disks consisted of cotton fabric (inner layer) and medical oilcloth (outer layer). The disks remained on the skin for 5 h. After this, the cotton disk and the inner side directed toward the skin and made of medical oilcloth were washed in saline. The washings were cultured on the surface of 5% Weitzinger's blood agar. The obtained results were compared to data on microbial contamination of the air environment of the chamber.

Samples of microflora of the air environment in the chamber were collected by the aspiration and sedimentation method into Petri dishes with 5% blood agar using a Krutov apparatus.

The cultures were put in an incubator for 2 days at 37°C . After incubation, we counted the colonies of microorganisms.

Results and Discussion

As can be seen from the data submitted in Table 1, there was a substantial increase in discharge of microorganisms from the upper respiratory tract in study No. 1, starting on the first day the subjects spent in the sealed chamber. When temperature and humidity in the chamber were increased, there was even more intensive discharge of microorganisms, as compared to the initial data. This process also continued when optimum conditions were provided in the chamber. At the last day of the study, the intensity of discharge of microorganisms from the subjects' upper respiratory tract increased by 22 times while breathing calmly and by 9 times when articulating, as compared to the initial period.

Table 1. Mean total number of microorganisms discharged by subjects in 10 min at different stages of the study (M±m)

Subject	Index	Before study	Study with			After study
			optimum habitat (1st-5th day)	elevated temp. & humidity (6th-20th days)	optimum habitat (21st-30th days)	
N-in	Respiration	30±12	180±42	300±48	320±24	18±12
	Articulation	105±105	230±30	370±70	470±115	75±25
Ts-vich	Respiration	6±2	82±26	160±30	440±150	5
	Articulation	55±25	145±30	250±40	330±100	10
P-ov	Respiration	24±6	92±26	250±32	250±56	8±6
	Articulation	15±35	280±110	250±35	290±75	120±50
Kl-in	Respiration	20±8	172±28	220±62	300±60	14±4
	Articulation	75±20	206±25	420±95	450±60	100±35
Total microbes per m ³ air in sealed chamber		350	5400±900	19 100±2 100	68 500±31 900	

The dynamics of microbial contamination of the air in the chamber developed in complete conformity with changes in intensity of discharge of microorganisms from the upper respiratory tract in study No 1 (see Table 1).

Thus, for the first 3 days of the study, microorganism content of the air environment in the chamber increased by 15 times; it increased by 55 times when temperature and humidity were raised and by 195 times at the end of the study, as compared to the base period.

Table 2 lists the results obtained in study No 2. As can be seen from these data, there was appreciable increase in migration of microorganisms from the upper respiratory tract during the subjects' stay in the sealed chamber, as was the case in study No 1; this pattern was particularly demonstrable in our study of processes of discharge of microorganisms during articulation. There were up to 2500 microorganisms discharged from the upper respiratory tract in 10 min when reading a standard text aloud.

The intensity of emission of microorganisms from the integument also increased at different stages of the study. One of these stages was characterized by restricting use of personal hygiene by the subjects; the second coincided with lowering the air temperature in the chamber to 16°C and increasing relative humidity to 75-80%.

The results of examining the microflora of the air in the sealed chamber in study No 2 (see Table 2) indicate that maximum microbial contamination of the environment was demonstrable during the period of restriction of personal hygiene measures.

Table 2. Mean quantities of total microorganisms discharged by subjects at different stages of study No 2 (M±m)

Index	Before study	Study with				After study
		optimum habitat	restricted personal hygiene	optimum habitat	ambient temp. 16±1, 75-80% humidity optimum habitat	
Microorganisms discharged during calm breathing (10 min)	23±10	177±73	295±84	317±182	159±86	25±10
Microorganisms discharged during articulation (10 min)	109±54	211±116	548±153	1530±632	725±379	114±69
Microorganisms disseminated from 25 cm ² skin (5 h)	410±292	586±546	1240±406	187±147	107±41	77±8
Total microorganisms per m ³ air	1700	3800	4700	3900	4700	

As can be seen from the data listed in Tables 1 and 2, exit from the sealed chamber upon termination of the studies was associated with a decrease in intensity of discharge of microorganisms from the upper respiratory tract and integument to the base level.

Thus, these studies revealed that the amount of microorganisms discharged into the environment from human integument increases substantially when people are confined to a closed area. While a mean of 19±8 microorganisms are discharged under ordinary living conditions from the upper respiratory tract of man when breathing calmly for 10 min, 113±47 are discharged during articulation for the same period of time and 243±150 microorganisms per 25 cm² skin in 5 h, the figures obtained when people are confined to a sealed area are 230±65, 415±106 and 728±309, respectively. When living conditions in the sealed area are more strenuous (elevation of temperature and ambient humidity, restricted personal hygiene), there is an even more marked increase in intensity of discharge of microorganisms. Evidently, the increase in microbial contamination of the upper respiratory tract and integument of people confined in a sealed area and cabin of functional spacecraft, reported in several studies [9, 10], is one of the causes of this finding.

The results of our studies revealed that there was usually a 15-30-fold increase in number of microorganisms in the nose, mouth and throat of subjects during their stay in the sealed chamber. Thus, in subject K1-in (study No 1), total number of microorganisms before the study constituted 3×10⁴ per sponge in the nose, 6×10⁷/5 ml washings from the mouth and throat, versus 1×10⁶ and 1.6×10⁹, respectively, by the end of the study. There was also significant

microbial contamination of the integument (50-100-fold), which reached 5×10^3 - 1×10^4 microorganisms per 25 cm² dorsal skin surface toward the end of the study.

On the basis of the above data, it can be concluded that the first stage of the mechanism of transmission of microorganisms, discharge from the body, is made easier when people are confined to a sealed area and as a result of the effects of some factors inherent in space flights (restricted use of personal hygiene measures). The quantitative indices submitted here, which characterize the intensity of discharge of microorganisms from the human integument, may be used in designing systems for purifying the atmosphere of manned spacecraft.

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ULTRASTRUCTURAL CHANGES IN CANINE HEPATOCYTES DURING CONTINUOUS CHRONIC EXPOSURE TO LOW DOSES OF GAMMA RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 65-69

[Article by L. A. Beshpalova, V. V. Shikhodyrov and V. S. Romanov, submitted 28 Jun 77]

[English abstract from source]

Electron microscopy of the liver of dogs exposed to chronic 6-year gamma-irradiation from the Co^{60} source demonstrated early changes in the hepatocyte structure at a relatively low dosage of 63 rad for 3 years. A comparative study of the submicroscopic reaction of hepatocytes of 3 groups of test dogs showed equally pronounced changes in the endoplasmatic reticulum vacuolar transformation balloon dystrophy. The heterogeneity of ultrastructural changes of different hepatocytes was probably associated with a simultaneous development of processes of injury, reparation and adaptation of intracellular structures during the long-term gamma-irradiation exposure. Parallel development of these processes assured reparative biosynthesis to maintain the normal hepatic function.

[Text] Light-optical studies of the dynamics of morphological changes in the dog liver with continuous exposure to low doses of gamma radiation, which simulated in magnitude and dose rate the probable radiation exposure in cabins of spacecraft, revealed development of dystrophic changes in the liver after 4 years, with accretion of a cumulative dose of 500 rad chronic radiation [1]. The radiation effect was more marked in the case of a combination of chronic and acute irradiation [2].

Our objective here was to investigate the main processes of impairment and recovery of hepatocytes of the same dogs on the submicroscopic level. The desirability of such a study is also related to determination of the minimum dose rate of chronic gamma radiation inducing ultrastructural changes in hepatocytes.

Material and Methods

Electron microscopic studies were conducted on 3 groups of dogs (6 animals in each group) exposed to ^{60}Co gamma radiation for 6 years in doses of

21 (1st group), 62.5 (2d group) and 125 rad (3d group) per year. Five dogs served as a control. The material was prepared according to Millonig, and a Japanese JEM-100B microscope was used to examine it.

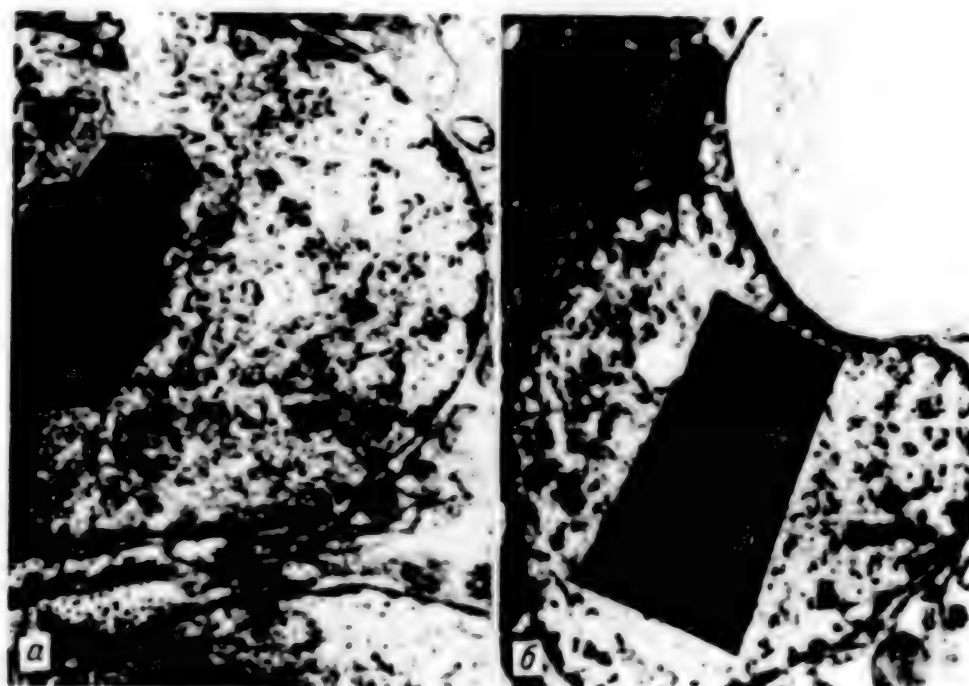


Figure 1. Intranuclear "crystalloid" type inclusions

- a) control, magnification 12,000×
- b) 6 years after chronic irradiation (deformation of nucleus by cytoplasmic vacuole), magnification 12,000×

Results and Discussion

A study of hepatocytes of control dogs over a 6-year observation period failed to demonstrate appreciable changes in ultrastructural organization. We almost always encountered isolated hepatocytes with markedly dilated ergastoplasm filled with fine granular substance. The presence of such "guard" cells in a state of hyperfunction was probably due to the functional heterogeneity of different hepatocytes [3]. There was an increase in number of diverse inclusions in the cytoplasm. In some nuclei, we found osmophilic elements in the form of crystals (Figure 1a). Some authors related formation of such inclusions to processes of cell aging [4].

Submicroscopic examination of the liver of experimental dogs, as compared to light optical examination, enabled us to demonstrate changes in hepatocyte structure with lower dose levels of chronic gamma radiation. The earliest changes were demonstrated after 3 years in the 1st group. The changes in the hepatocytes were essentially of the same type in all experimental dogs.

When we analyzed the intracellular structures, we were impressed by the reaction of the system of the endoplasmic reticulum, which was manifested by varying degrees of dilatation and vacuolar transformation (Figure 2a). As a rule, vacuolization began in the central region and gradually extended to the periphery of the cell. Occasionally, the vacuoles occupied virtually the entire cell, totally impairing its cytoarchitectonics and deforming the nucleus (Figure 1b).

Development of so-called ballooning dystrophy, which began on the periphery of the cells and gradually extended to the middle, was observed with another form of hepatocyte lesion (Figure 2c). This process was expressed by attenuation of electron density (clearing) of cytoplasm, reduction of cytogranules of glycogen, degradation and dissociation of endoplasmic reticulum membranes. The membranes of the smooth endoplasmic reticulum broke down into fine blebs and fragments, which formed aggregations in the form of "stacks" occupying different sized areas. Concurrently with degranulation of the reticulum, in the cytoplasm there was an increase in amount of free ribosomes and polyribosomes. As a rule, next to clear, altered hepatocytes there were virtually always hepatocytes with dark cytoplasm, sometimes containing 2-3 nuclei. In such hepatocytes there was marked hyperplasia of granular reticulum, mainly around the mitochondria, as well as in the perinuclear regions (Figure 2c). Such a structural change could probably signify a constant change from intracellular protein synthesis of the extracellular type (with degranulation of the endoplasmic reticulum, increase in free ribosomes and polysomes) to intracellular synthesis during the period of repair of lesions. Conversely, hyperplasia of granular endoplasmic reticulum in optically dense (dark) cells was indicative of a change from protein synthesis of the intracellular type to the "export" type [5, 6].

Thus, in the course of 6 years of continuous exposure to gamma radiation, the ergastoplasmic membranes presented greater lability of processes of reorganization in all three groups of experimental animals. The complicated changes in this membrane system, manifested differently in different hepatocytes, were apparently an ultrastructural expression of competition between different types of cellular biosynthesis, depending on the stage of damage or repair of cells.

The reaction of the mitochondrial system of hepatocytes was essentially stereotypical with different dose levels of chronic gamma radiation, and it was characterized by consolidation of the mitochondrial matrix with marked reduction of cristae, which was indicative of depressed mitochondrial energy and decline of overall level of redox phosphorylation [7, 8]. Territorial

redistribution of mitochondria was observed, depending on the degree of development of intracellular edema; the mitochondria were pushed away by dilated cisterns of endoplasmic reticulum to intact parts of the cytoplasm. There was a decrease in number of mitochondria in clear hepatocytes, whereas it increased by more than 10 times per unit surface in adjacent, more electron dense ones (Figure 3a).

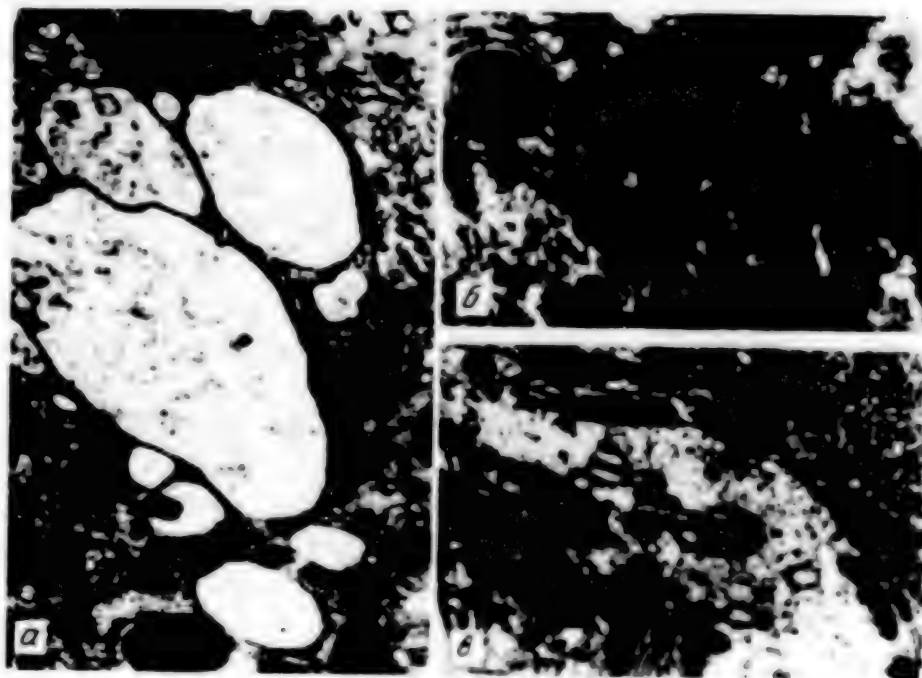


Figure 2. Reaction of endoplasmic reticulum

- a) vacuolar transformation, magnification 14,000×
- b) hyperplasia of granular reticulum, magnification 20,000×
- c) "balloon" dystrophy, magnification 10,000×

In the biliary parts of hepatocytes, as well as at sites of hydropic lesion to the cytoplasm, there was activation of the lysosomal system with accumulation in it of fragments of organelles and pigmented inclusions of the lipofuscin granule type (Figure 3c). Such autophagosomes--"cytolysosomes" (varying in degree of maturity)--were a typical finding in hepatocytes of dogs exposed to radiation for a long time. On the basis of current conceptions of lipofuscin as a metabolic product of unsaturated fats, many

authors interpret accumulation thereof in cells as an indicator of impairment of normal course of fat metabolism in the liver [9, 10].

Many pigment granules, myelinoid figures and lipid inclusions (see Figure 2a; 3c, d) appeared in all experimental dogs, mainly at the late experimental stages (5-6 years). The inclusions varied in shape, and this was probably consistent with differences in their chemical composition [11].

The structural changes in hepatocyte nuclei were mainly secondary in nature and related to changes in the cytoplasm. Most often, there was a change in its outlines, as a result of compression of endoplasmic reticulum by the dilated vacuoles. In some nuclei of experimental animals, we find the same "crystalloid" inclusions as in control dogs after exposure to radiation for 5-6 years (see Figure 1b).

At the late experimental stages, regardless of dosage of gamma radiation, all dogs presented signs of cholestasis in the form of dilatation of biliary capillaries, with signs of edema and partial reduction of microvilli (see Figure 3a), as well as constriction of Disse's spaces.

The Kupffer cells reacted somewhat differently. Activation thereof, related to increased phagocytic function, was manifested by enlargement of these cells, appearance of many cytoplasmic processes and intracellular phagocytized particles (Figure 3e).

Thus, electron microscopic studies of the liver of dogs exposed to long-term external gamma radiation revealed early changes in hepatocyte structure after delivery of a relatively low level of doses constituting 63 rads/year. Analysis of submicroscopic reactions of hepatocytes over a 6-year period revealed that, in the case of continuous irradiation, processes of adaptation, damage and repair of ultrastructures may take place simultaneously and this, of course, makes it difficult to pinpoint the stages of damage and recovery. Such a contingency of processes could have determined the apparent heterogeneity of the ultrastructural reaction, which was manifested by varying degrees of destruction of intracellular organelles in some hepatocytes and compensatory hyperplasia thereof in others.

The results of this investigation enable us to assess the nature of metabolic disturbances in the liver of dogs exposed to long-term radiation. It may be assumed that processes of oxidative phosphorylation were the first to be depressed, as a result of which there was a change in state of membranes of the endoplasmic reticulum, impaired utilization of glycogen, distorted protein synthesis and increased glycogenolysis. This obtained electron microscopic confirmation by formation of extensive areas of agranular profiles of endoplasmic reticulum, which appeared in areas where glycogen disappeared. There was only secondary impairment of lipid metabolism (lipid inclusions in hepatocyte cytoplasm). The validity of our hypothesis is confirmed by assessment of carbohydrate-energy, protein and lipid metabolism in the same dogs [12]. At the same time, the results of this investigation revealed



Figure 3. State of hepatocytes in dogs of the 3d group after 5 years of chronic exposure to gamma radiation

- 1) light and dark hepatocytes, 12,000x
- 2) lipofuscin granules, 20,000x
- 3) myelinoid figure in bile capillary lumen, 20,000x
- 4) Kupffer cell with phagocytized particles in cytoplasm, 10,000x

that the observed compensatory and adaptive reorganization of intracellular structures in the course of long-term exposure to gamma radiation made possible repair biosynthesis in damaged hepatocytes and was very important to intracellular hyperplastic processes for preservation of proper function of hepatic tissue as a whole.

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RUSH NUTS (CYPERUS ESCULENTUS) AS A SOURCE OF VEGETABLE OIL IN A CLOSED LIFE SUPPORT SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 70-74

[Article by M. P. Shilenko, G. S. Kalacheva, G. M. Lisovskiy and I. N. Trubachev, submitted 28 Jun 77]

[English abstract from source]

The cultivation schemes, productivity, total biochemical, lipid in particular, composition of nodules of chufa (*Cyperus esculentus*) were studied, using a phytotron. Upon continuous illumination chufa yielded a high total productivity and a satisfactory coefficient of economic effectiveness (not less than 50%). Chufa nodules have an optimal ratio of proteins, carbohydrates and fats containing essential fatty acids. To meet man's requirements for vegetable oils and essential fatty acids, it is necessary to produce daily 150-200 g dry chufa nodules which are quite acceptable as a dietary ingredient.

[Text] Higher plants can play the part of reclaimers of oxygen, water and food in a human life support system. The most specific function of higher plants, which cannot presently be replaced by physicochemical processes, is the biosynthesis of a wide spectrum of foodstuffs required by man. For this very reason, when selecting higher plants for closed life support systems, the criterion of satisfying the nutritional needs of man should be advanced to first place. Actual satisfaction of man's requirements referable to all foodstuffs is possible only by developing a multicomponent unit of higher plants for closed systems.

Oil-producing plants were not used in previous studies involving the use of higher plants. For this reason, still open is the question of furnishing vegetable oils to man, in particular essential fatty acids. In selecting plants to be included in the higher plant unit, we considered sunflowers, flax, soya, peanuts, rush nuts and others.

Data in the literature [1-3] and our own experience in growing oil-producing plants revealed that sunflowers, flax and mustard, which are widespread under field conditions, have a rather low yield of edible portion in view of the

large share of stems, roots and leaves in the harvest, as well as due to minimal or no use of cakes that are left after extracting oil from seeds. We consider soybeans and peanuts unsuitable for use in a closed system by virtue of their specific developmental features (short day requirement, fertilization and development of ovaries of peanuts). According to the results of the studies, the rush nut (*Cyperus esculentus*), a plant of the Cyperaceae family, is rather promising. Rush nuts multiply vegetatively, forming many edible tubers, 15-20 mm in length and 5-10 mm in thickness, on the roots. The oil they contain is similar in quality to olive and peanut oil. The tubers contain 20-25% (dry mass) oil, up to 60% carbohydrates and about 8% protein.

Methods

Experiments involving cultivation of rush nuts under artificial light were conducted in phytotrons of the experimental Bios-3 system [4] in order to determine the productivity of the plants and coefficient of economic usefulness of biomass, reaction of plants to continuous exposure to light, optimum density of plants, optimum harvesting time, overall biochemical composition and lipid composition as related to cultivation conditions.

We raised the rush nuts hydroponically on a 10-12-cm layer of claydite submerging them in Knopp nutrient medium after 6 h. They were exposed to light from DKS-TV-6000 lamps around the clock, with intensity of illumination of 200-230 W/m² PAR (photosynthetic active radiation). Air temperature was 23-25°C and humidity 80-85%.

We kept a record of the harvest in two replicas of cultivation, with 70-30 plants in each (depending on the area of nutrition thereof).

In the biochemical analyses, we calculated the crude protein content by multiplying total nitrogen (according to Kjeldahl) by a coefficient of 6.25. Carbohydrate analysis was made by the anthrone method; carbohydrate fractions were determined according to Belozerskiy and Proskuryakov [5]. Oil was extracted with a mixture of alcohol and ether (3:1 by volume) and assayed by weighing. Fatty acids were isolated after saponification, using acidulated methanol for methylation. Methyl ethers of fatty acids were recorded on a chromatograph. Recording conditions: 2.4 m column length, 6 mm diameter, 20% polyethylene glycol adipate on zeolite as filler, 50 ml/min velocity of carrier gas and 180°C temperature. An ionization-flame detector was used.

Results and Discussion

Rush nuts planted using presprouted tubers develops slowly for the first 10-15 days, then begins to form bushes rapidly with many narrow, almost vertically directed leaves that make good use of intensive light. Most of the tubers begin to form at the age of 45-50 days, but they ripen later, in 60-70 days. This is associated with formation of new runners and new tubers.

Table 1. Rush nut harvest as related to area of plant nutrition and duration of vegetative period

Vegetation time, days	Plant feeding area, cm	Wet wt., g/m ²		Dry wt., g/m ²		Dry mass productivity, g/m ² per day		Tubers in harvest, %	Light W/m ²
		total bio-mass	tubers	tot. bio-mass	tub.	total bio-mass	tubers		
70	10×10	12195	3650	3613	1963	50.2	27.3	54.3	231
72	10×15	9097	2871	2785	1558	38.7	21.6	56.3	205
72	15×15	11025	3108	3255	1636	45.2	23.3	50.6	215
90	10×10	14503	4484	4556	2476	50.6	27.6	54.2	231
90	10×15	12380	4003	3836	2155	42.6	23.9	55.4	205
90	15×15	112111	3739	3528	2059	39.2	22.6	56.6	215
120	10×10	13949	4671	4594	2632	38.3	21.9	57.3	—

The yield of rush nuts and productivity (per day) in experiments involving different duration of vegetation and different density of plants are shown in Table 1. As can be seen in Table 1, the best results were obtained with a nutrition area of 10×10 cm. Enlargement of the feeding area led to some reduction of harvest. The harvest of rush nuts accumulated intensively for 3 months and had not stopped building up by the 90th vegetation day, since harvesting at this age revealed that in the overall yield of edible product there were up to 8.6% young immature tubers. However, extension of vegetation to 120 days led to a relative decrease in productivity. In 90 days of vegetation, in the variant with a feeding area of 10×10 cm, the mean coefficient of useful effect of photosynthesis of rush nuts constituted 4.8% of incident photosynthetically active radiation, and more than half this figure (2.9%) was referable to the economically useful part.

The experiments revealed that rush nuts are as good as wheat in economic productivity. Thus, mean productivity of wheat raised in the same devices with illumination of 145 W/m² PAR constituted 50.5 g/m² per day (in dry form) including 17.7 g/m² edible biomass, whereas the figures for rush nuts exposed to light of 231 W/m² PAR were 50.6 and 27.6 g/m², respectively.

The overall biochemical composition of rush nut tubers (without lipids) is listed in Table 2. Crude protein constituted 6–8%, and it was virtually unrelated to density of planting and time of harvesting. Amino acid analysis revealed that the proteins of rush nuts are characterized by a low level of essential (with the exception of lysine) amino acids, which diminishes their nutritional value. The predominant amino acids are arginine (51% of total content), aspartic and glutamic acids (7% each) and lysine (6%). When scaled to protein, there is about twice as much lysine in rush nuts as in wheat. Carbohydrates (without cellulose) constituted 55–61% dry tuber mass. In ripe tubers there was prevalence of polysaccharides of the starch type

(40-49%), and water-soluble sugars constituted 7-15%. In immature tubers the sugar content was considerably higher (preferable to starch).

Table 2. Biochemical composition of rush nut tubers (% dry substance)

Vegetation time, days	Plant feeding area, cm	Crude protein	Water-soluble sugars	Carbohydrates			Total carbohydrate (without cellulose)
				starch	hemi-cellulose	cellulose	
70	10×10	7.5	25.1	28.0	3.2	6.0	56.3
72	15×10	6.9	8.2	48.2	4.7	5.7	61.1
72	15×15	6.9	14.1	40.0	3.9	5.8	58.4
90*	10×10	6.3	32.3	27.9	3.7	5.1	63.9
90**	10×10	7.5	4.7	49.5	2.8	4.6	57.0
90	10×10	6.3	7.5	45.8	3.8	5.5	57.1
90	10×15	7.5	12.3	44.3	4.1	5.8	60.7
90	15×15	8.1	7.9	48.6	4.1	5.8	60.6
120	10×10	6.9	9.0	39.5	6.5	4.0	55.0

*Green [unripe] tubers.

**Only ripe tubers.

Table 3. Rush nut lipids and fatty acid composition thereof

Variant of experiment	Vegetation time, days	Plant feeding area, cm	Total lipids (% of dry substance)	Fatty acids (% lipids)	Fatty acids (% of total fatty acids)				
					palmitic	palmitic	stearic	oleic	linoleic
I	70	10×10	17.5	60.0	18.2	0.4	1.7	67.6	12.2
II	72	15×10	19.3	76.9	17.2	0.5	2.0	68.9	11.4
III	72	15×15	21.8	84.0	16.2	0.5	3.0	70.3	10.3
IV	90*	10×10	3.0	60.6	24.1	0.5	1.9	47.0	26.3
V	90**	10×10	21.3	88.3	16.2	0.3	3.7	69.6	10.1
VI	90	10×10	20.1	82.1	17.0	0.5	3.2	69.0	10.3
VII	90	10×15	20.7	82.4	14.7	0.5	3.5	71.1	10.0
VIII	90	15×15	21.8	85.3	17.2	0.4	3.2	68.7	10.3
IX	120	10×10	21.6	83.0	14.4	traces	3.9	71.3	10.4

*Green tubers.

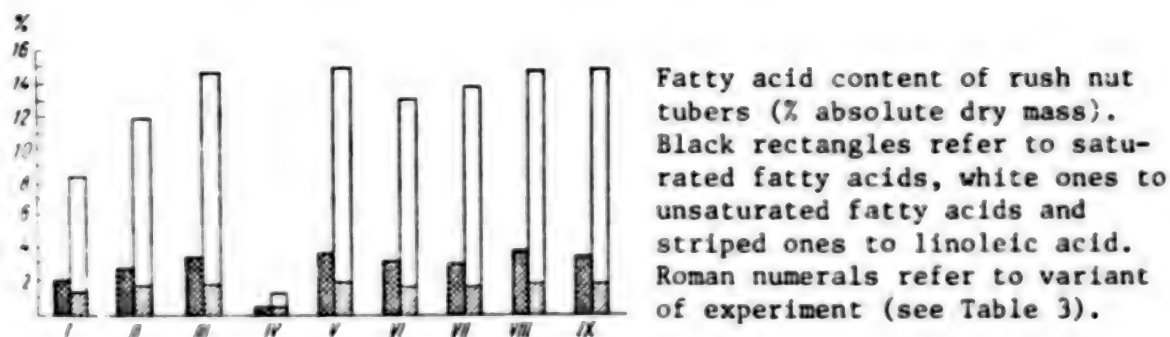
**Only ripe tubers.

Also noteworthy is the fact that rush nut tubers contain 6.2 µg/g vitamin B₁ (versus 3.7-6.1 in wheat grain) and 5.7 µg/g vitamin B₂ (0.6-3.7 in wheat grain).

Total lipid content of rush nut tubers constituted 19.3-21.8% dry substance (Table 3), with the exception of unripe ones, in which only 3% was referable

to lipids. The acids of rush nuts are represented chiefly by the saponifiable fraction, which constitutes over 80% in ripe tubers (see Table 3). This fraction contains three unsaturated and two saturated fatty acids. Oleic acid is the prevalent unsaturated acid, constituting 69-71% of total fatty acids. Linoleic acid, which is essential, constitutes 10%. The relative palmitic acid content does not exceed 0.5%. Saturated fatty acids are represented by palmitic (14-17%) and stearic (3.5%) acids.

The fatty acid composition of young tubers is characterized by higher relative linoleic and palmitic acid content than in ripe ones, while the share of oleic and stearic acids is lower (see Table 3).



The Figure illustrates levels of different fatty acids as a function of feeding area and degree of maturation; the results are given after scaling to absolute dry mass. Analysis of these data shows that the fatty acid content is affected mainly by the degree of tuber maturity, rather than planting density. The figure also shows that essential linoleic acid constitutes 3.0-3.3% in dry tubers. Consequently, 150-200 g rush nuts can furnish the complete daily human requirement of essential fatty acids and vegetable oil.

The results of the study of Yu. N. Okladnikov et al. [6], who included up to 130 g rush nuts (in flour used to bake bread and cakes [or cookies], in soup and dairy products) in the daily diet of people, demonstrated the acceptability of this foodstuff.

The high productivity of rush nuts when exposed continuously to light, the large share of edible substance in the harvest (50-60%), high vegetable oil content (along with proteins and carbohydrates) with essential fatty acids and satisfactory nutritional qualities warrant recommending this plant for inclusion in the higher plant unit, along with others (wheat, vegetables), and for testing in experimental closed life support systems for man.

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METHODS

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A METHOD OF DEFINING THE OPTIMUM LEVEL OF IONIZING RADIATION FROM DETERMINATE SOURCES DURING SPACE FLIGHTS

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[Article by A. V. Kolomenskiy and V. A. Sakovich, submitted 4 May 77]

[Text] The random nature of solar bursts, which are associated with fluxes of corpuscular radiations and, accordingly, the differences in expected radiation dose during space flights make it desirable to consider the probability of a certain adverse effect in man, which we shall refer to hereafter as risk, as a possible criterion of radiation safety [1, 2]. At the same time, in order to plan protection against radiations present in a prespecified time mode (we shall call these sources determinate), we must define the permissible dose, D_d (or dose rate) of such determinate radiations over the entire flight.

We describe here a method of determining this dose on the assumption that radiation protection on a spacecraft consists of two elements: protection against probable and determinate sources. The criterion of radiation safety in the form of maximum risk $R \leq R_0$ is obtained with a minimum weight of such protection: P_p [subscript p refers to probable] + P_d [subscript d refers to determinate] $\rightarrow \min$. It is also possible to extend this method to a large number of sources, each with its own protection, unrelated to other sources.

Galactic cosmic radiation, the radiation belts of earth and onboard nuclear installations are determinate sources. The probabilistic nature of radiation may be due not only to solar bursts, but difference in time spent in fields of radiation from determinate sources.

If the probability of an adverse effect $F(D)$ as a function of dosage and probability of exceeding specified dose $\eta(D)$ are known, the risk would be:

$$R = \int_0^{\infty} \frac{dF}{dD}(D) \eta(D) dD = - \int_0^{\infty} F(D) \frac{d\eta}{dD}(D) dD. \quad (1)$$

For the assumptions made as to composition of protection, condition of optimum thereof has the following appearance:

$$\frac{dR}{dP_d} = \frac{dR}{dP_p} \quad (2)$$

In the presence of both probabilistic and determinate sources:

$$\eta(D) = \begin{cases} 1 & \text{with } D \leq D_d \\ \eta_p (D - D_d) & \text{with } D > D_d \end{cases} \quad (3)$$

therefore

$$R = - \int_{D_d}^{\infty} F(D) \frac{d\eta_p}{dD} (D - D_d) dD = - \int_0^{\infty} F(D_p + D_d) \times \\ \times \frac{d\eta_p}{dD} \frac{p}{p} (D_p) dD_p \quad (4)$$

Using only solar bursts [subscript b in formulas] as the probabilistic source, we shall write down as in [3]:

$$D_p = D_b = \eta K_b (\delta s), \quad (5)$$

where ϕ is the flux of protons of solar bursts and $K_b (\delta s)^*$ is the dose of a single flux as a function of thickness of radiation protection. Then:

$$R = - \int_0^{\infty} F(\eta K_b + D_d) \frac{d\eta_b}{d\phi} d\phi \quad (6)$$

and further:

$$\frac{dR}{dP_d} = - \int_0^{\infty} \frac{dF}{dD} \frac{d\eta_b}{dD} \frac{dD}{dP_d} dD_b = \mu_d^{ef} D_d \int_0^{\infty} \frac{dF}{dD} \frac{d\eta_b}{dD} dD_b \quad (7)$$

$$\frac{dR}{dP_p} = - \int_0^{\infty} \frac{dF}{dD} \frac{d\eta_b}{dD} \eta \frac{dK_b}{dP_p} d\phi = \mu_b^{ef} \int_0^{\infty} \frac{dF}{dD} \frac{d\eta_b}{dD} K_b dD_b \quad (8)$$

$$\mu_i^{ef} = -d \ln D_i / dP_i \quad (9)$$

is the effective coefficient of attenuation of the dosage of the i th source by its protection [4]. Making the notation:

*Translator's note: subscripts and/or superscripts keyed as follows in all formulas: p) probable; d) determinate; b) burst; s) protection ["shelter"]; ef) effective.

$$D_{b}^{ef} = \int_0^{\infty} \frac{dF}{dD} \frac{d\eta_b}{dD} D_b dD_b \cdot \int_0^{\infty} \frac{dF}{dD} \frac{d\eta_b}{dD} dD_b \quad (10)$$

we obtain the correlation between optimum of combined protection [4]:

$$\mu_{dD}^{ef} = \mu_b^{ef} \mu_b^{ef} \quad (11)$$

where D_b^{ef} is, as we see, related not only to K_b , but to D_d .

Simultaneous solution of equations (4) and (10) should yield the values of D_d and δ_s , if we consider that μ_b^{ef} is known and unrelated to the value of D_d . However, it is difficult to find this solution, since [5]:

$$\eta_b(D) = 1 - \int_0^D \sum_{k=0}^{\infty} e^{-\lambda T} \frac{(\lambda T)^k}{k!} f_k(D_k) dD_k, \quad (12)$$

$$\text{where } f_k(D_k) = \int_0^{\infty} f_{k-1}(D_{k-1}) f_1(D_k - D_{k-1}) dD_{k-1}$$

with $k \geq 2$, k the number of the burst, D_k the total dose of k bursts, $f_1(D)$ the density of distribution of probability of dose D in one burst, with $f_0 = 1$, and λ the mean incidence of bursts. For this reason, we must simplify equations (4) and (11). For this purpose, let us write $F(D)$ in the following form:

$$F(D) = 1 - \sum_{i=1}^n A_i e^{-\omega_i D}, \quad (13)$$

consequently,

$$\frac{dF}{dD} = \sum_{i=1}^n A_i \omega_i e^{-\omega_i D}. \quad (14)$$

Then equations (4) and (11) will include $\int_0^{\infty} \omega_i e^{-\omega_i D} f_1(D) dD$.

which, having the shape of a generating function of moments of convolution of multiplicity k and f_1 , constitutes [6]:

$$\left[\int_0^{\infty} e^{-\omega_i D} f_1(D) dD \right]^k.$$

As a result, we shall have:

$$\begin{aligned} R &= 1 - \sum_{i=1}^n A_i e^{-\omega_i D} d \sum_{k=0}^{\infty} e^{-\lambda T} \frac{(\lambda T)^k}{k!} \left[\int_0^{\infty} f_1(D) e^{-\omega_i D} dD \right]^k = \\ &= 1 - \sum_{i=1}^n A_i e^{-\omega_i D} d \exp \left[-\lambda T \left[1 - \int_0^{\infty} f_1(D) e^{-\omega_i D} dD \right] \right], \quad (15) \end{aligned}$$

i.e.,

$$R = 1 - \sum_{i=1}^n B_i (\delta S) e^{-\omega_i D d}$$

Analogously

$$\int_0^{\infty} \frac{dF}{dD} \frac{d\eta b}{dD} dD b = \sum_{i=1}^n C_i (\delta S) e^{-\omega_i D d} \quad (16)$$

where $C_i = -\omega_i B_i$.

As for $\int_0^{\infty} \frac{dF}{dD} \frac{d\eta b}{dD} D b dD b$, let us present $D b$ in the following form:

$$D b = \lim_{\omega_s \rightarrow 0} [(1 - e^{-\omega_s D b}) / \omega_s] \text{ with } \omega_s \rightarrow 0.$$

Then:

$$\begin{aligned} \int_0^{\infty} \frac{dF}{dD} \frac{d\eta b}{dD} D b dD b &= - \sum_{i=1}^n A_i \omega_i e^{-\omega_i D d} \lim_{\omega_s \rightarrow 0} \frac{1}{\omega_s} \times \\ &\times \left\{ \exp \left[-\lambda T \left(1 - \int_0^{\infty} e^{-\omega_i D} f_1(D) dD \right) \right] - \exp \left[-\lambda T \times \right. \right. \\ &\quad \left. \left. \times \left(1 - \int_0^{\infty} e^{-(\omega_i + \omega_s) D} f_1(D) dD \right) \right] \right\}. \end{aligned}$$

Hence

$$\int_0^{\infty} \frac{dF}{dD} \frac{d\eta b}{dD} D b dD b = \sum_{i=1}^n C_i e^{-\omega_i D d} \lambda T \int_0^{\infty} f_1(q) q K b e^{-\omega_i q K b} dq. \quad (17)$$

As a result, the optimality condition acquires the following form:

$$\frac{\mu_d^{ef}}{\mu_b^{ef}} = \frac{\lambda T K b (\delta S) \sum_{i=1}^n C_i e^{-\omega_i D d} \int_0^{\infty} q f_1(q) e^{-\omega_i q K b} dq}{D d \sum_{i=1}^n C_i e^{-\omega_i D d}} \quad (18)$$

and it is a system of transcendental equations (15) and (18), rather than integral equations (4) and (11), that must be solved.

If equation (18) is written in a somewhat different form:

$$\frac{\mu_d^{ef}}{\mu_b^{ef}} = \frac{\bar{D} b}{D d} \cdot \frac{\sum_{i=1}^n C_i e^{-\omega_i D d} \left[\int_0^{\infty} q f_1(q) e^{-\omega_i q K b} dq / \int_0^{\infty} q f_1(q) dq \right]}{\sum_{i=1}^n C_i e^{-\omega_i D d}}. \quad (19)$$

it becomes clear that the integration process of solving the above transcendental equations should begin with calculation of D_d from the following equation:

$$\mu_d^{ef} D_d = \mu_b^{ef} D_b.$$

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BRIEF REPORTS

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PSYCHOPROPHYLAXIS OF FATIGUE AND FUNCTIONAL CARDIOVASCULAR DISEASES IN PILOTS BY MEANS OF SELF-CONDITIONING

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5,
1979 pp 77-78

[Article by A. N. Gurov, submitted 23 Mar 78]

[Text] The great physical and emotional tension inherent in flight work, and the effects of various adverse flight factors (temperature changes, lowering of partial oxygen pressure, restriction of movements, gravitational influence, etc.) sometimes lead to development of early fatigue and functional cardiovascular diseases. For this reason, it is an important element of the system of psychological, moral and political pilot training to increase mental and physical resistance to various flight factors [1].

Methods

The pilots studied ranged in age from 22 to 42 years, and they were divided into three groups: the first consisted of individuals subject to rapid fatigue (32 people); the second consisted of individuals suffering from neurocircular dystonia of the hypertensive type (19 people) and the third consisted of individuals with neurocirculatory dystonia of the hypotensive type (17).

The physician held group classes with each group twice a week, for 10-20 min each time, during which he explained the significance of autogenic training and rules for using exercises, the daily performance of which by the pilots independently (morning, day and evening, 5-10 min at a time) should result in a state of autogenic induction. Before starting the independent exercises and 6 months later, we recorded arterial pressure, heart rate, intensity of perspiration, tremor and electrocardiograms on all individuals.

At the first 5-7 classes, there was substantiation of the efficacy of verbal influences, the possibility of attaining active dilatation of extremital vessels with them and hence the sensation of warmth in these vessels. After this, we began to make practical use of verbal activity in order to eliminate fatigue and induce normalization of arterial pressure.

Results and Discussion

Analysis of the obtained data revealed that all of the pilots present a decrease in feeling of fatigue after ordinary loads, appearance of a sensation of vigor after the sessions, positive attitude toward autogenic conditioning and active desire to control any malaise after 6 months of regular practice.

The Table summarizes the results of the obtained changes in arterial pressure and pulse, which were processed by the method of variational statistics with calculation of means (M \pm m).

Changes in arterial pressure and heart rate related to self-training

Group of subj.	Arterial pressure				Heart rate	
	before self-train.		after self-train.		before self-training	after self-training
	systolic	diastolic	systolic	diastolic		
1	124.3 \pm 1.3	72.1 \pm 0.7	125.1 \pm 1.7	71.7 \pm 1.7	82.3 \pm 2.8	73.8 \pm 1.9
2	142.7 \pm 2.6	84.4 \pm 3.5	130.1 \pm 1.3	75.3 \pm 1.5	72.8 \pm 1.7	70.1 \pm 2.3
3	117.0 \pm 3.1	61.1 \pm 4.3	120.4 \pm 2.2	64.4 \pm 3.3	80.6 \pm 2.8	74.3 \pm 1.5

In the first group of subjects, there was negligible change in arterial pressure in the course of training, with slowing of heart rate, excessive perspiration and tremor; sensation of fatigue after considerable mental and physical loads occurred less often.

In the second group, we observed persistent decline of arterial pressure ($P > 0.05$), slowing of heart rate ($P > 0.05$) and disappearance of tremor in the course of autogenic conditioning. In 12 people in this group, we demonstrated periodic sinus extrasystoles on the KEG; they disappeared in 10 of these cases with autogenic training and remained unchanged in 2. After 4 and 6 months of regular practice, 4 pilots of this group were deemed to be in good health at their routine check-up by the medical flight commission, which was performed at the hospital.

In the third group, arterial pressure (both systolic and diastolic) rose, with some decrease in heart rate and disappearance of tremor.

The data referable to 68 pilots who performed the exercises for 6 months indicate the efficacy of the method of autogenic conditioning in the modification of specific organ training as a means of preventing fatigue and functional cardiovascular diseases in pilots. The systems we used for autogenic conditioning can be used to prevent fatigue and functional cardiovascular diseases in flight personnel.

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USE OF SHORT-ARM CENTRIFUGE TO PREVENT DECONDITIONING WHEN IMMERSSED IN WATER (ACCORDING TO H-REFLEX)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 78-79

[Article by B. I. Zborovskaya, submitted 15 Nov 77]

[Text] A study was made of the possibility of using periodic rotation on a short-arm centrifuge (SAC) as a means of preventing the adverse effects of immersion.

Methods

Healthy volunteer subjects participated in this study; they were immersed in water for 3 days. We estimated endurance of head-pelvis (+Gz) accelerations on a centrifuge with a radius of 7.25 m before and after immersion. The rate of build-up of accelerations constituted 0.2 units/s, time of exposure to accelerations of +3Gz constant in magnitude and direction constituted 5 min. Each subject was submitted to +3Gz after pure immersion and immersion combined with periodic rotation on a SAC, where accelerations of +0.8 Gz, +1.2 Gz or 1.6 Gz were generated for 60 min twice a day (first series) and for 40 min 3 times a day (second series). The subjects were positioned on the SAC in such a manner as to have the axis of rotation traverse the region of the bridge of the nose. In all, we conducted 61 tests involving 12 subjects. Under these conditions, we tested neuromuscular functions by the methods of the H (Hoffmann) reflex and electromyography. The H-reflex was elicited by electric stimulation of the tibial nerve in the region of the right popliteal fossa using square-wave single pulses. Pulse duration was 0.7 ms and frequency 0.33 Hz. Electromyograms were recorded by the conventional method from the right femoral quadriceps, right anterior tibial muscle and left soleus. A computer was used to process the electromyograms.

Results and Discussion

The H-reflex method makes it possible to assess activity of spinal α -motoneurons, the role of which is to induce or restrict movement [1]). It was

previously noted [2] that with G forces of +3 Gz there are two types of changes in the H-reflex: initial inhibition at the start of exposure to +3 Gz, with subsequent recovery and alleviation at the start of +3 Gz [sic], which is characterized by increase in amplitude of the reflex. Recovery and stabilization of amplitude of the H-reflex in the "aftereffect" of +3 Gz occurred in the 2d-3d min. The "initial" inhibition of the H-reflex observed in our studies is apparently determined mainly by a change in level of afferent influences related, in particular, with increased extrafusal (?) tension of the tested flexor of the foot (soleus) and thus induced activation of tendon receptors of Golgi. Subsequent restoration of amplitude of the H-reflex with +3 Gz could be related to relative relaxation of the tested muscle.

Alleviation of the H-reflex at the start of exposure to +Gz is perhaps related to reciprocal excitatory effect in the presence of marked tension of the anterior tibial muscle. Increased excitability of spinal α -mo. neurons, manifested by lowering of threshold of eliciting the H-reflex, occasionally by replacement of the "primary" inhibition of the H-reflex by alleviation thereof, was demonstrated under the influence of +3 Gz after immersion. Restoration of H-reflex amplitude in the aftereffect period occurred by the 7th-10th min. The decline of threshold of eliciting the H-reflex after immersion is indicative of increased excitability of spinal α -motoneurons [3], and this was also observed previously in the case of immersion in water for 24 and 120 h [4, 5].

In subjects who did not experience entirely the specified mode of exposure to accelerations (+3 Gz, 5 min), after immersion (regardless of type of changes in the H-reflex at the start of exposure), before termination of exposure to +3 Gz we observed "secondary" inhibition of the H-reflex, which coincided with marked reduction of amplitude of vascular pulse in the lobule of the ear. The positive effect of periodic rotation on the SAC for the purpose of preventing deconditioning of the neuromuscular system was assessed on the basis of time of restoration of amplitude of the H-reflex in the aftereffect period and appearance of secondary inhibition of the H-reflex with exposure to +3 Gz. In 76% of the cases, there was early recovery of H-reflex amplitude (1st-3d min of aftereffect) with exposure to +3 Gz after immersion combined with SAC when using G forces of +1.2 Gz for 40 min 3 times a day, and the same was observed in 62% of the cases with the use of G forces of +1.6 Gz for 60 min twice a day. The fewest number of cases of secondary inhibition of the H-reflex was observed after immersion combined with 1.6 Gz for 60 min twice a day.

These investigations do not permit us to evaluate with sufficient certainty the pathological mechanism of secondary inhibition of the H-reflex; however, the simultaneous marked decrease in amplitude of vascular pulse in the conchal lobule warrants the assumption that there is a change in level of supraspinal influences, which is indirectly attributable to the state of cerebral circulation. At present, it is known [6] that the use of periodic rotation on a centrifuge with an arm 7.25 m in size increases resistance

of the body to head-pelvis accelerations after immersion, in particular it reduces significantly the development of hemodynamic disturbances.

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COURSE OF ALTITUDE CAISSON DISEASE IN DOGS EXPOSED TO ACCELERATIONS

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[Article by V. I. Prodin and I. N. Chernyakov, submitted 9 Feb 78]

[Text] Situations may arise in high-altitude and space flights where man is exposed to the combined or successive effects of low pressure and G forces, with signs of altitude decompression sickness: maneuvering an aircraft in a depressurized cabin, descent from orbit in a depressurized compartment of a spacecraft, etc. It is unquestionable that the hydrostatic pressure of body fluids, which changes in the presence of accelerations, shifting of these fluids and deformation of soft tissues would affect the evolution of gas bubbles that were formed during altitude decompression, as well as development of symptoms of caisson disease.

There are no data in the literature that are directly related to this matter. At the same time, there are works [1] indicating a correlation between the size of the gas bubbles and hydrostatic pressure. It was shown that as a gas bubble shifts to the region of elevated hydrostatic pressure its volume decreases. In the light of these data it was interesting to track the dynamics of development of symptoms of altitude decompression sickness against the background of changing hydrostatic pressure due to accelerations.

Methods

Experiments were conducted on mongrel dogs. Altitude decompression sickness (ADS) was induced by "lifting" the animals to an "altitude" of 5000 m in a pressure chamber, with a physical load (running on a treadmill) after pressaturation with nitrogen while breathing air at pressure of 4-5 atm for 1-3 h [2].

Animals with marked symptoms of ADS (paresis and paralysis of the limbs, respiratory and cardiac functional disorders, general depression) were divided into two groups. The natural outcome of the sickness was observed in animals of the first group (eight experiments) for 3 days after "altitude" decompression. After 3 days, the animals were sacrificed for morphological studies. The second group of animals (nine experiments) with symptoms of

ADS were rotated on a centrifuge for 10 min, with chest-back accelerations of 8 units. The intervals between start of development of ADS and rotating the animals constituted 15-30 min (4 cases), 1.5-2.5 h (4 cases) and 24 h (1 case). The animals were under observation for 3 days after rotation.

Results and Discussion

Two of the animals in the first group recovered. In one case, the signs of general depression and paraplegia of the hind legs, which were observed for the first hours after decompression, gradually regressed, and total recovery was observed on the 3d day. In the second experiment, the dog presented only monoplegia of the left hind leg, which disappeared entirely after 3 days. In a third experiment on the same dog, after altitude decompression we observed paresis of the same left extremity, which progressed unexpectedly and severely: on the 2d day there was development of paraplegia of the hind legs with serious respiratory and cardiac disorder. The dog was sacrificed in an agonal state. These cases of total recovery from severe clinical signs of ADS and lethal outcome with relatively moderate early symptoms confirm the statements [3, 4] to the effect that it is difficult to prognosticate the outcome of the disease on the basis of the initial stage of its development.

In the other five experiments with animals of the first group, we observed consistent progression of ADS symptoms; as a result, 2 animals died in the first hour after altitude decompression, as a consequence of massive air embolism; in three cases monoplegia and paraplegia progressed into paraplegia and tetraplegia with further worsening of the animals' general condition. These data were indicative of development of persistent ADS symptoms in most animals with the method we used to simulate this disease.

The results of the second series of experiments turned out to be quite remarkable, where the animals with persistent ADS symptoms were rotated on a centrifuge. In two cases, rotation worsened the condition severely in dogs with signs of paraplegia and tetraplegia, general depression, respiratory and cardiac functional disorder. This finding can be readily explained. Hypoxia induced by massive air embolism of pulmonary and coronary arteries in the presence of altitude decompression was aggravated as a result of respiratory and circulatory disturbances, which developed under the influence of accelerations [5].

At the same time, in seven other experiments, instead of the expected aggravation of the animals' condition after rotation, we observed total or partial removal of ADS symptoms. It should be noted that such an effect was observed with milder forms of the sickness, paresis or paralysis of one extremity, when the animals' general condition was satisfactory, they ate and moved independently (on three legs). After rotation, the animals began to put weight on all four legs, including the one that had been stricken.

The fact that G forces were able to curb local symptoms of ADS apparently requires further investigation. It may be assumed that there is elevation of hydrostatic pressure of body fluids in the distal parts of the body, in relation to the vector of G forces, which compresses gas bubbles, under the influence of G forces during rotation. This reduces deformation of tissues, normalizes circulation in stricken regions and restores impaired functions of the extremities.

At the same time, the findings may be opposite in the proximal parts of the body, and the outcome of caisson disease could ultimately depend on the localization of gas bubbles and shifting thereof.

During rotation of animals at G forces of 8 units, the increment of hydrostatic pressure in the dorsal region constituted about 100-150 mm Hg. An increase in pressure by this amount or even less could arrest the pain symptoms of ADS in some cases, when they develop in man in a pressure chamber at "high altitude" [2, 4, 6].

However, it would be wrong to reduce the ADS symptom curbing effect of G forces solely to compression of gas bubbles. It is a known fact that the gas bubbles can be persistent [stable], and so can the symptoms of ADS with considerably higher degrees of compression [4]. Evidently, under the influence of G forces, in addition to compression there is deformation of gas bubbles, as well as migration and destruction of membranes thereof. Muscular tension, present when the animal experiences motor excitement during rotation, as well as intensification of respiration and circulation, which occur during rotation when the animal's general condition is satisfactory after altitude decompression, are also instrumental in these effects.

Of course, these results do not constitute a substantiation for practical recommendations on the treatment of ADS symptoms by rotation on a centrifuge. They are interesting primarily because they demonstrate the positive effect on the body of such an extreme factor as G forces under specific conditions.

The experimental results also enable us to expound the hypothesis that the presence of symptoms of mild forms of ADS in a crew member does not constitute a mandatory contraindication for performance of a stage of a flight mission related to exposure to accelerations.

On the basis of these data it may also be assumed that formation of gas bubbles in the lower limbs during a space flight in weightlessness, as well as development of ADS when atmospheric pressure is low, will apparently occur faster as a result of absence of hydrostatic pressure of body fluids.

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INVESTIGATION OF ALVEOLOARTERIAL DIFFERENCE FOR OXYGEN AND CARBON DIOXIDE
WHEN BREATHING HIGH-DENSITY GAS MIXTURES

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1979 pp 81-83

[Article by L. A. Bryantsev, A. G. Dianov, V. V. Isayenko, A. V. Suvorov
and R. I. Finogenova, submitted 22 Mar 78]

[Text] Our objective here was to determine the alveoloarterial difference for oxygen and carbon dioxide when breathing high-density gas mixtures. In addition, unlike previous studies, we deemed it important to investigate under these conditions respiratory reactions uncomplicated by the effect of anesthesia; for this reason, we conducted the experiments on nonanesthetized animals pretrained to breathe through a mask.

Methods

Experiments were conducted on dogs weighing 9.5 kg each.

One month before the experiments, catheters were imbedded in the aorta and ostium of venae cavae, which were used to take blood for tests.

We used SF₆ as neutral diluent gas. The inhaled gas mixture of SF₆ and O₂ (or atmospheric air in control tests) was delivered through a mask and valve box from a Douglas bag. The gas mixture was prepared just prior to the test; the oxygen concentration in it constituted 20.9±1% (the density of a respiratory mixture of SF₆ and O₂ with 21% O₂ is 4.21 times higher than the density of air).

We conducted 16 experiments in all: 10 using SF₆-O₂ for breathing and 6 with the use of air for breathing (control).

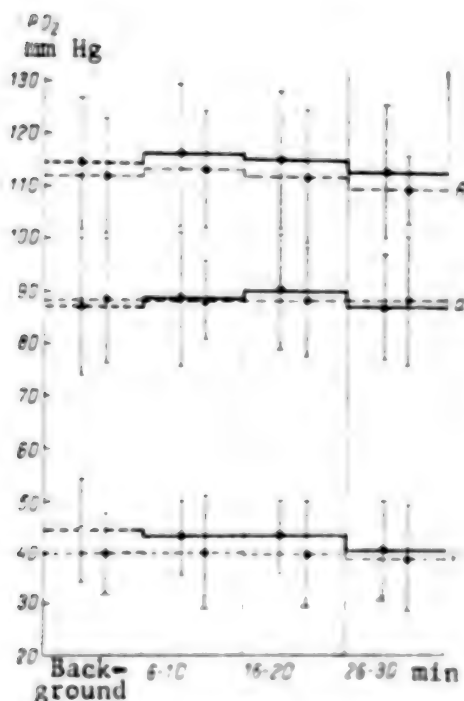
In each experiment, we determined the following main parameters: respiration rate (f), minute volume (V_E), O₂ and CO₂ concentration in alveolar air using a capnograph and OM-11 gas analyzer. Volumes of exhaled air were collected in Douglas bags and assayed with a GSB-400 gas counter. The rest of the parameters of external respiration and gas exchange, determined by the Douglas-Haldane method, were calculated from these indices: respiratory [tidal] volume (V_T), O₂ and CO₂ tension in alveolar air (P_{AO_2} and P_{ACO_2}), alveolar

ventilation (V_A), dead space (V_D), respiratory coefficient (R), coefficient of oxygen uptake (KO_2), oxygen uptake ($\dot{V}O_2$) and carbon dioxide output ($\dot{V}CO_2$). Analysis of inhaled and exhaled gas mixtures for O_2 and CO_2 content was made on the OM-11 analyzer and capnograph. Blood tests were made using the AME-1c micro-Astrup. Blood was collected under vaseline oil directly from the catheters in the aorta and ostium of the venae cavae. We measured O_2 and CO_2 tension in arterial and venous blood (P_{aO_2} ; P_{aCO_2} ; P_{vO_2} ; P_{vCO_2}).

Determination was also made of alveoloarterial difference ($A-aPO_2$ and $a-APCO_2$) from the values of O_2 and CO_2 tension in alveolar gas and blood.

Each experiment was conducted in two stages: first we determined the above-mentioned parameters of respiration, exchange of gases and blood in the base state before breathing the gas mixture; at the second stage we determined all parameters three times during 30-min respiration of SF_6-O_2 mixture (in the first 10 min, second 10 min and third 10 min).

The results of all experiments were processed by the method of Student-Fisher. In most cases, we used the method of pair-by-pair comparison of base and end (between 20th and 30th min) values in each experiment.



Graph of PO_2 changes in alveolar air (A), arterial blood (a) and venous blood (v) during 30-min respiration of SF_6-O_2 gas mixture (solid line) and air (dash line)

Results and Discussion

The Figure illustrates the main results of the experiments. As can be seen, there is no difference from the control ("air") series in PO_2 of alveolar air, as well as arterial and mixed venous blood when breathing a mixture of SF_6 and O_2 . During 30-min breathing of the SF_6-O_2 mixture, alveoloarterial difference for oxygen constituted 20.4 ± 5.3 mm Hg; it was 25.8 ± 7.6 mm Hg when breathing air. The 5.4 mm Hg difference was statistically unreliable ($P > 0.05$). The same applies to alveoloarterial difference for carbon dioxide: $a-APCO_2$ constituted 3.04 ± 0.73 mm Hg with the SF_6-O_2 mixture and 5.43 ± 2.55 mm Hg when breathing air ($P > 0.05$).

A comparison of base levels of respiratory gases in blood to the end data in each experiment revealed that the SF_6-O_2 breathing mixture does not lead to statistically reliable changes in P_{aO_2} , P_{aCO_2} , P_{vO_2} and P_{vCO_2} .

Alveolar ventilation, calculated from $P_A\text{CO}_2$, also failed to demonstrate reliable differences.

However, a reliable increase in respiratory volumes and slower respiration were observed with the use of the $\text{SF}_6\text{-O}_2$ mixture. Reflex deepening and slowing of respiration made it possible, as we know, to overcome resistive resistance, which had increased in the dense medium, with less exertion of respiratory muscles [1-5].

On the basis of these experiments, it may be assumed that inclusion of inert gas of high density in respiratory mixtures, at normal atmospheric pressure, does not elicit any appreciable changes in transport of oxygen and carbon dioxide.

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TOXIC EFFECTS OF CHEMICALS IN THE ALTERED GAS ENVIRONMENT OF PRESSURIZED CHAMBERS

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[Article by G. I. Solomin, submitted 14 Apr 77]

[Text] The monograph of V. V. Kustov, L. A. Tiunov and G. A. Vasil'yev [1] presents a survey of data on the combined effect on man and experimental animals of toxic agents combined with other environmental factors. There has been insufficient publication of works dealing with the nature of the toxic effects of chemicals in an altered gas environment and, in particular, against the background of lowered barometric pressure [1-5].

Our objective here was to investigate the toxic effect of chemicals that are the products of gas emission from polymers on experimental animals in an altered gas environment, as this relates to spacecraft cabins.

Studies were conducted with the use of 1,4-dioxane, ethyl acetate and isopropyl benzene. These agents are often identified in the air of manned compartments of spacecraft [6].

Methods

We conducted 26 series of experiments on 224 white mice weighing 25-30 g, with different concentrations of the agents both under ordinary conditions on the ground and in an artificially created gas environment of a pressure chamber (barometric pressure was lowered to 520 mm Hg, while oxygen level was held at a 40% level). Each experiment lasted 2 h. The experiments were conducted in a 260-liter pressure chamber under static conditions. The concentration of chemicals in the air of this chamber was measured by weighing and gas chromatographic methods. Air samples were collected at the end of each experiment.

The levels of median lethal concentrations (LC_{50}), as well as LC_{10} and LC_{90} , which are widely used in industrial toxicology for determination of parameters of acute toxicity of toxic agents, served as the indicators of

toxic effects of the chemicals. All of the digital data were submitted to statistical processing by the method of probit analysis [7].

Results and Discussion

The Table lists the results of studies made in order to determine the median lethal concentrations of the toxic substances studied (1,4-dioxane, ethyl acetate and isopropyl benzene, in experiments on white mice).

Data referable to determination of LC_{50} of dioxane, ethyl acetate and isopropyl benzene in experiments in a normal and altered gas environment

Agent	Experimental conditions	Concentration mg/liter	Deaths (out of 8 mice in group)	Lethal concentration		
				LC_{16}	LC_{50}	LC_{84}
1,4-dioxane	Ground	55 59 64 74	1 4 7 8	55	60 (55,5—64,4)	65
	Altered	46 62 65 72	0 3 5 8	57	63 (60—67,3)	69
Ethyl acetate	Ground	19 21 35 42 48	0 1 4 5 8	23	33,5 (28,7—41,4)	47,5
	Altered	35 39 43 49 53	0 2 3 6 8	36	45 (40,9—47,3)	52,4
Isopropyl benzene	Ground	20,1 22 27,6 32	0 2 6 8	21,6	25 (22,5—27,3)	30,5
	Altered	25 27,6 32 37	0 2 6 8	26,2	30,5 (27,1—30,9)	35,8

As can be seen in the table, the levels of median lethal concentrations of all three agents tested, as well as such indices as LC_{16} and LC_{50} , obtained in experiments under normal barometric pressure are lower than the data obtained in an altered gas environment against the background of lowered barometric pressure. This is indicative of some attenuation of the toxic effects of 1,4-dioxane, ethyl acetate and isopropyl benzene on experimental animals in an altered gas environment at lowered barometric pressure. In the tests with ethyl acetate and isopropyl benzene, this attenuation of the toxic effect is apparent from the fact that the median lethal concentrations (LC_{50}) demonstrated in the tests under ordinary ground-based conditions (P 760 mm Hg, 21% O_2) were on the level of nonlethal concentrations demonstrated in the experiments at low barometric pressure. The same pattern is demonstrable when we compared other parameters of the animals' reaction (LC_{16} and LC_{01}).

Thus, the study of the toxic effect of the above chemicals at low barometric pressure (down to 520 mm Hg) with concurrent increase in oxygen content to 40% (PO₂ 208 mm Hg) revealed some attenuation of their toxic effect. This was manifested by an increase in levels of lethal concentrations.

Our findings coincide with data in the literature [5], the authors of which report a lower mortality rate among animals exposed to nitrogen dioxide and ozone against the background of lowered barometric pressure. The milder course of poisoning or decline of lethal concentrations in our experiments is apparently related to the increase in oxygen content and slowing of the process of sorption of agents in the body at lower barometric pressure. However, for definitive determination of the effect of chemicals combined with ambient factors, which could be present in an actual space flight, further investigations are required.

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EFFECT OF HYPOXIA ON ATPASE ACTIVITY OF THE BRAIN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 85-87

[Article by L. B. Buravkova, E. S. Mailyan and Ye. A. Kovalenko, submitted 24 Oct 77]

[Text] At the present time it is a known fact that tissular hypoxia elicits changes in energy metabolism and damage to membrane structures of the cell. Impairment of bioenergetic processes leads to progressive decline in concentration of macroergic compounds [1, 2]. It has been demonstrated that, in the presence of profound hypoxia, there is depression of tissular respiration and dissociation thereof from phosphorylation [3-5]. Intensification of glycolytic processes during this period [6] cannot fully compensate for the decrease in oxidative phosphorylation, for which reason the ATP level drops. Since the ATP level depends on the correlation between synthesis and hydrolysis thereof in the cell, it is deemed important to investigate its ATPase activity.

According to the data in the literature, rarefaction of the atmosphere up to an altitude of 7000 m elicits an increase in intensity of hydrolysis of ATP [7]. However, when rats are lifted to an altitude of 9000 m for 90 min, a decrease is observed in ATPase activity in the membrane fraction of the cerebral hemispheres [8], whereas no change was demonstrated in rate of ATP hydrolysis in a brain homogenate even 4 h after ligating the common carotid artery of rats [9]. Such contradiction of data prompted us to undertake a comprehensive study of this enzyme in the presence of different degrees of hypoxia in different species of animals differing in resistance to acute hypoxia.

Methods

We conducted our study on 35 mongrel, male albino rats weighing 200-300 g and 70 male CBA mice weighing 25-30 g. Acute hypoxic hypoxia was produced in a pressure chamber with rarefaction of atmosphere to the appropriate altitudes (40 m/s rate of ascent). The mice were lifted to altitudes of 4000, 6000 and 8000 m for 5 min, and 10,000 and 11,000 m until respiration stopped. The rats were lifted to 12,000 and 14,000 m; they were brought down

after onset of respiratory arrest as demonstrated on a pneumogram. After bring the animals down as rapidly as possible (15 s), they were decapitated; we extracted the cerebral hemispheres and placed them in a cooled solution (0-4°C; 0.25 M) of saccharose, 5 mM tris-HCl, 2 mM EDTA, pH 7.4); blood was washed off and the preparation homogenized to 1:10 (weight:volume).

Fractions were isolated using a TsiR-1 centrifuge at 2°C by a method previously described [10]. ATPase Mg^{2+} activity was determined from the increment of phosphate in a medium of the following composition: 10 mM tris-HCl, 5 mM $MgCl_2$ and 5 mM ATP. To the sample we added 0.2-0.3 mg protein and incubated it for 15 min at 37°C. The reaction was stopped by adding 0.5 ml cold 10% trichloroacetic acid solution. The samples were kept on ice for 10 min; settled protein was separated and determination was made of inorganic phosphate (P_i) in the supernatant using the method of Lowry and Lopez in the modification of V. P. Skulachev [11], while protein was assayed according to Lowry [12].

Results and Discussion

When lifting mice to different altitudes, we found that with rarefaction of atmosphere at 4000 and 6000 m there was virtually no difference in ATPase Mg^{2+} activity, as compared to the control (Figure 1). Starting at an altitude of 8000 m, the activity of this enzyme increased by 57%, and at an altitude of 10,000 m by 79%. However, upon reaching an altitude of 11,000 m, which is the "ceiling for CBA mice, according to our data, there was a sharp drop of enzyme activity: by 57% as compared to the control and to one-third the activity at 10,000 m. These changes are statistically reliable ($P < 0.001$).

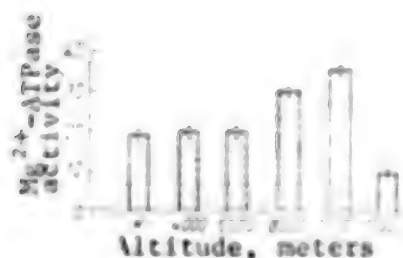


Figure 1.

Mg^{2+} -ATPase activity of CBA mouse brain under normal conditions (K) and when lifted to different altitudes (μg P_i /mg protein/15 min)

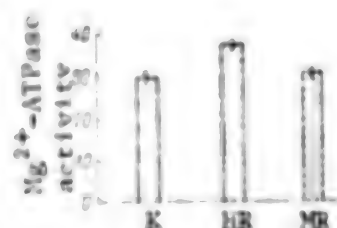


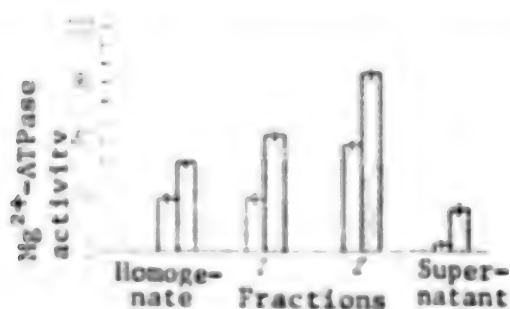
Figure 2.

Mg^{2+} -ATPase activity of the brain of highly and minimally hypoxia-resistant rats (HR and MR) in the presence of acute hypoxia (μg P_i /mg protein/15 min)

It was established that, when lifted to 12,000 m, most rats die on the average within 100 s after reaching this altitude. In this group of animals, enzyme activity was 27% higher ($P < 0.01$) than in the control group (Figure 2). A few animals died considerably later at 12,000 m, within a mean of 9 min 40 s. In

these rats, the increase in ATPase activity of the brain was statistically unreliable, as compared to control animals. Consequently, in animals that are highly resistant to hypoxia, activity of Mg^{2+} -ATPase of cerebral hemispheres was lower at high altitude than in animals with minimal resistance. This is consistent with data obtained by O. S. Klimenko [13] for mitochondria and nuclei isolated from the brain of albino rats.

In a separate series of experiments (20 animals), ATPase activity of the brain was studied with elevation of rats to the altitude ceiling (14,000 m). Under normal conditions, as shown in Figure 3, hydrolysis of ATP in fraction II (containing mitochondria) was almost twice the level in fraction I (containing nuclei and fragments of nerve fibers) and 12 times greater than in fraction III (soluble). Immediately after the ascent to 14,000 m, however, we observed the following: enzyme activity increased by 69% in the brain homogenate; ATPase activity doubled in fraction I, increased by 68% in fraction II and by almost 6 times in fraction III. Thus, an increase in ATPase activity under hypoxic conditions was observed in all tested fractions.



The above results warrant the belief that increase in activity is the most typical reaction of Mg^{2+} -ATPase to acute hypoxia. The results of lifting mice to 11,000 m are the only exception to the demonstrated pattern, and no explanation for this was found. Our studies revealed that a change in ATPase activity of the mouse brain after "ascents" is demonstrable for the first time at an altitude of 8000 m. We know from the literature that it is expressly at this rarefaction of the atmosphere that PO_2 of brain tissue comes close to a critical level [14].

The increase in enzyme activity in the presence of acute hypoxia may be due to the following factors: dissociation of oxidation and phosphorylation [3, 4], which, as we know, elicits an increase in ATPase activity; activation of phospholipase A, which, by impairing phospholipid structure, perhaps also decreases Na^+K^+ -ATPase on the outside of the membrane and activates Mg^{2+} -ATPase, an enzyme situated on the inside of the membrane [7]. Phosphorylase A is activated by free fatty acids [15], the amount of which, as we know, increases in the presence of hypoxia [16, 17]. Ca^{2+} ions, the amount of which in the cell also increases in the presence of hypoxia [2], are activators of this enzyme.

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BOOK REVIEWS

UDC: 656.7+629.78]-051:159.9(049.32)

NEW BOOK DEALS WITH EXPERIMENTAL PSYCHOLOGICAL RESEARCH IN AVIATION AND COSMONAUTICS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 87-88

[Review by A. A. Krasovskiy of the book "Eksperimental'no-psikhologicheskiye issledovaniya v aviatsii i kosmonavtike" by G. T. Beregovoy, N. D. Zavalova, B. F. Lomov and V. A. Ponomarenko, Moscow, Nauka, 1978]

[Text] At the present time there is no need to describe the role and significance of engineering psychology and ergonomics. The scientific and technological revolution and the rapid development of automated control systems have advanced problems of interaction between man and machine to the ranks of the most timely areas of theory and practice. Research dealing with engineering psychology holds a leading place in scope and depth. This can be attributed both to the particular complexity and responsibility of pilot and cosmonaut activities and historically formed traditions.

The Soviet scientific and engineering literature in the field of aviation and space psychology includes some excellent books and a significant number of articles in the periodic press.

The Soviet literature has now been enriched with another monograph written by prominent specialists in this field.

Before discussing the contents of this book, it must be stressed that this reviewer is not a specialist in psychology and, specifically, engineering psychology. The contents of the monograph are analyzed from the vantage point of an engineer who is concerned with questions of onboard control systems and complexes.

The first chapter, which deals with the psychological bases of operator work serves as a general theoretical introduction to the book. The authors cite some interesting data of the UN Technical Committee, according to which the share of automated systems in developed countries increased from 12 to 60% in 15 years (from 1960 to 1975). In this same period, the share of purely manual labor decreased from 76 to 8%.

In the general discussion of the activities of an operator, much attention is given to Marxist-Leninist conceptions in the area of individual labor and such basic concepts of engineering psychology as information model, conceptual model, image-goal, levels of regulation of activity, skills and ability, planning, etc. The authors touch upon the physiological bases as well of the problem of planning operator activity.

Further, the book deals with specific problems and questions of aviation and space engineering psychology. What is valuable in this monograph is that the presentation of rich, specific experimental material is accompanied by theoretical generalizations and important conclusions, while the experiments themselves often pursue the goal of substantiating specific conceptions. There are some valuable materials and conclusions derived from psychological analysis of man's performance during space flights and aircraft piloting processes, as well as engineering psychological studies of emergency and malfunction situations.

The system of views presented in the monograph of the role of a pilot in an automated onboard aircraft control system, interaction between the crew and onboard equipment also presents great interest, though it is debatable in some of its aspects.

In a somewhat simplified form, we can describe these views as follows: It is unlikely that "absolutely"* reliable automatic control systems (ACS) will be developed in the next decade. The main role of the pilot is to back up ["reserve"] the ACS. In order to perform the functions of a "hot" reserve, the pilot must implement not only active monitoring, but active movements, i.e., he must be constantly "present" in all of the control systems. This condition is met by "combined" control, when the pilot works concurrently with the machine. The logic of these views and experimental substantiation thereof for the present cannot be denied. Still, in our opinion, joint control should be viewed as a temporary measure.

Development of multiprocessing onboard computer systems, spare actuating devices and remote electric systems for the control of rudder surfaces (instead of mechanical wiring) determine the routes and grounds for drastically increasing reliability. Virtually absolute reliability is a mandatory prerequisite for introducing the most promising systems of active control of flying vehicles, systems that provide for damping aeroelastic oscillations, piloting under conditions of static instability, lowering the rate of spending the resources of the glider, decreasing discomfort due to variedirectional accelerations, etc. Incidentally, it is virtually impossible for man to spare [reserve] active control systems, since the spectrum of signals of these systems is beyond the human transmission band. Thus,

*We refer to the level of reliability, at which the probability of dangerous malfunction of the ACS is smaller than the probability of destruction of the glider, controls, incapacity of the crew, etc.

development of technology will make it impossible and unnecessary for man to save [reserve] the lower ("internal") control systems.

It is a very different matter with regard to higher control levels. We must concede that there is complete validity to the view reiterated in the monograph concerning the need for the pilot to play an active role, the inadmissibility of transforming him into an accessory of the machine. In future systems, this active role should, in our opinion, be performed on an intellectual, verbal-thinking level.

Some of the active actions of a pilot, which will be retained for all of the foreseeable future are control of the onboard complex itself, with due consideration of the actually formed situation, detection and recognition of goals, particularly nonstationary ones with little contrast, choice of optimum means of using weapons and criterion for automatic optimization of a flight maneuver and mode. The pilot, as the commander of a highly sophisticated, adaptable and partially self-organizing onboard system, plays a rather active, creative role, capable of bringing moral and psychological satisfaction to a man on a flying vehicle of the future.

Considerable attention is devoted in the book to concepts of the personal and human factors. While we agree that there is a definite need for the concept of human factor, we should like to comment on the fact that the authors go to some extremes in their judgements, in the heat of polemics. The concept of personal factor is important not only in screening, training, medical and psychological monitoring, but as an element of the system of education, discipline and responsibility. Unquestionably, there is a need to develop a scientific approach to identification of mistakes, separation of personal and human factors.

The statement (p 101) that organization of the pilot's work place is presently the prerogative of engineers is somewhat exaggerated. In practice, already at the stage of the mock-up commission and the numerous subsequent tests, cabin equipment is discussed and refined by pilots and experts. The main flaw is that this process is essentially empirical, without a broad theoretical foundation as yet. The authors are quite right in drawing attention to the need to plan pilot activity, as well as for in-depth ergonomic evaluation at the very earliest stage of developing a flying vehicle.

The last chapter of the book demonstrates convincingly the great applied implications of psychological studies in aviation and cosmonautics.

On the whole, this monograph, like several previous publications, is indicative of the leading positions of Soviet engineering psychology. The book will, no doubt, elicit deserved interest among a wide circle of engineers, pilots and scientists.

PRESSING PROBLEMS OF SPACE BIORHYTHMOLOGY DISCUSSED IN NEW BOOK

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 pp 88-90

[Review by V. A. Doskin and N. A. Lavrent'yeva of the book "Aktual'nyye problem kosmicheskoy bioritmologii" by S. I. Stepanova, Moscow, Nauka, 1977, 311 pages]

[Text] As we know, the achievements in the basic sciences serve as the foundation for successful development of applied research. In this respect, the space sciences are in the lead; using the achievements of world-wide science, they are developing at a rapid pace and enriching many scientific directions.

For this reason, all works dealing with the study of space are becoming the object of the closest attention among the most varied specialists. This 23d volume of the scientific publication, "Problems of Space Biology," deals with biorhythmology. It was written by the well-known Soviet biorhythmologist, S. I. Stepanova, and it is entitled "Pressing Problems of Space Biorhythmology."

Evaluation of the functional state of the human body at different points in time is the most important task of human biorhythmology, including space biorhythmology. At the same time, evaluation of the functional state of the human body is one of the key problems of medical science. When prescribing some treatment or other, determining the possibility of working under extreme conditions, assessing the work and rest schedule and rationalizing nutrition, a physician must assess the functional state of man and grade it, to the extent this is possible, as poor, good and optimum. Such gradation is substantially easier to make with the use in medicine of the rhythmometric approach developed by biorhythmology. Consideration of consistent changes in the functional state of man, which are related with his biological clock, makes it possible to differentiate between the distinctive features of reactions to a load, as well as to assess the reserve capabilities of the body.

Numerous years of observations made by the author demonstrate convincingly the importance of the rhythmometric approach to evaluation of the functional

state of the human body. Occasionally, examination of the course of human biological rhythms makes it possible to detect changes therein, so-called desynchronosis. All disturbances of the body leading to disease start because of disruption of timing of different functions, so-called internal desynchronosis.

S. I. Stepanova demonstrated convincingly that internal synchronization of daily (more precisely, circadian, from the latin, circa--about and dia--day) rhythms of different physiological functions and biochemical parameters constitutes an optimum state of the body. It is very apparent from the material submitted by S. I. Stepanova that the circadian rhythm is important to the human body. One can realize this by merely counting the functions (there are about 300) that change in a daily pattern.

As she develops the theoretical premises formulated by the well-known Soviet biorhythmologist, B. S. Alyakrinskiy, S. I. Stepanova, in her analysis of desynchronosis as a phenomenon, makes a distinction between "internal" and "external" desynchronosis, the latter referring to a discrepancy between vital processes and astronomic time. Physicians in different specialties often observe this phenomenon.

Characterizing desynchronosis as the main form of circadian disorder, she demonstrates the qualitative differences in sleep cycle disorders among night and split-shift workers, as compared to circadian changes related to transmeridional flights. It is observed that, in spite of the apparent adjustment of blue and white collar workers to different shifts, their life is contrary to the biological rhythm. As a result, various diseases (gastric and neurological) appear, and they are demonstrable primarily among those who adjust poorly to shift work. Thus, on the one hand desynchronosis is one of the early signs of disease and, on the other hand, having appeared as a result of disruption of the customary schedule of the day, it could itself become the cause of different diseases.

S. I. Stepanov, developing the conception of the human body as a complex rhythmic system, demonstrates that the state of the circadian system of man is a reliable criterion of his general condition, which makes it possible to derive some very important conclusions to medical practice as to the time of administration of drug and other therapy, work capacity reserves of the human body, etc.

We cannot fail to concur with the author that desynchronosis is a manifestation of the general adaptation syndrome. The recommendations of S. I. Stepanova pertaining to organization of labor under extreme conditions are based on this theoretical foundation. The book is very timely, since the generalizations it contains go beyond space science, and they are of definite value to organization of labor of shift and night workers, pilots of high-speed airliners and individuals in other occupations.

Of theoretical importance is the question posed by the author as to the possible range of expansion of the customary 24-hour day for man. What is the optimum length of a work day for man? How long should he rest? S. I. Stepanova finds an answer to this question by means of unique studies dealing with man's adjustment to days differing in length. These studies enabled the author to expound the hypothesis of informational-energetic cost of the daily cycle.

In essence, the conception of constancy of information-energy cost of the daily cycle refers to the fact that the amount of information received by man and energy expended is a constant parameter. With increase in duration of the daily cycle, the information-energy cost per hour should decrease and with decrease in duration of the daily cycle it should increase. If man is beyond the range of customary time indicators (sensors), the duration of the daily cycle is determined by the level of his physical and mental activity: the lower this level, the longer the circadian cycle should be, and vice versa. On the basis of this thesis, the author demonstrates the possible range of change in the daily cycle.

An adjunct to this hypothesis is the theoretical conception of possibility of expanding the biorhythmic stereotype, which was developed on the basis of the works of B. S. Alyakrinskiy. This conception deals with the individual properties of the body with respect to adhering to a stable daily schedule, with deviations in the range of 1-2 h. The author has called this interval the zone of the biorhythmological stereotype, since fluctuations of position of phases within this range do not disrupt rhythmic processes. Here too, the author backs up her conclusion concerning the individual capacity of people to adjust to a new rhythm of life. Thus, individuals with a wide zone of biorhythmological stereotype adjust more easily. This conclusion is quite important to occupational medical consultations and occupational screening, which take up a significant place in the work of a practicing physician.

Of direct interest to practicing physicians is a section dealing with the prevention of desynchronization, where the author demonstrates convincingly that a wisely planned work and rest schedule is the principal means of preventing desynchronization.

Special mention must be made of a chapter dealing with analysis of the main biorhythmic types of individuals. S. I. Stepanova arbitrarily makes a distinction between three types of people, labile, inert and intermediate; she demonstrates the adaptation capacities of each type to unusual time-related conditions or rapid changes in daily schedule. These data serve as the basis for biorhythmological screening of cosmonauts. Biorhythmological screening, even of cosmonauts, is a thing of the future, but the logic scheme thereof is also applicable to other occupations with an extreme component. As a result of screening, high and stable efficiency [work capacity] should be achieved under extreme conditions.

The book ends with a description of the prospects of scientific research in the field of space biorhythmology. This book will enrich substantially the knowledge of any physician, and it will be instrumental in progress in the main branches of medical science.

CURRENT EVENTS

UDC: 613.693(043.5):016

DOCTORATES CONFERRED

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 5, 1979 p 90

[Article by editorial board]

[Text] Following are the doctoral dissertations dealing with the specialty of "Space and Aviation Medicine," which were approved by the USSR High Degree Commission in 1978:

"Pathogenesis of Disturbances of Calcium Metabolism in Mineralized Tissues During Long-Term Hypokinesia," by A. I. VOLOZHIN (Institute of Biomedical Problems, USSR Ministry of Health, 25 Aug 78).

"Kinetics and Regulation of Fluid-Electrolyte Metabolism in Man and Animals During Hypokinesia," by V. P. KROTOV (Institute of Biomedical Problems, USSR Ministry of Health, 21 Apr 78).

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